ANNALS
OF
OTOLOGY, RHINOLOGY
AND
LARYNGOLOGY

VOL. 63 JUNE, 1954 No. 2

XXIV

PATHOLOGIC CHANGES OF THE SKIN OF THE EXTERNAL AUDITORY CANAL IN CHRONIC OTITIS MEDIA AND MASTOIDITIS

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A large number of skin specimens from the lining of the external auditory canal were assembled over a period of years in connection with an integrated study of the etiology, pathology, and treatment of diseases of this structure. Included among the specimens, collected largely at the time of fenestration and mastoid surgery, was a group obtained from 40 patients with chronic suppurative otitis media and mastoiditis. As the study of this material progressed, it became apparent that these skin specimens were not normal, but showed many consistent and typical histo-pathologic changes. It is the purpose of this paper to describe the microscopic changes of the skin of the external auditory canal in patients with suppurative otitis media and mastoiditis.

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This research was performed under Contract AF 33(038)28643 with the USAF School of Aviation Medicine, Randolph Field, Texas.

MATERIAL AND METHODS

Forty specimens of the skin of the external auditory canal were removed during the performance of radical mastoidectomies. In most of these cases chronic drainage from the middle ear had existed for many years. The tissue was cut in serial sections of 6 μ thickness and alternate sections were stained with hematoxylin and eosin. The unstained sections were subsequently stained with trichrome (Masson) and by the Romanowsky technique.

OBSERVATIONS

Epidermis: All sections show a pronounced thickening of the stratified squamous epithelium. Keratinization is comparable to that observed on the exposed skin surfaces (Fig. 1). Parakeratosis is commonly found. In an occasional area, the horny layer is elevated, leaving an intra-corneal space (Fig. 2). Intra- and intercellular edema are frequently observed (Figs. 2 and 3). The rete pegs are often elongated. Leukocytes can sometimes be seen infiltrating the epidermis (Fig. 3). Occasionally the caliber of excretory ducts and hair shafts seems to be diminished and plugs of keratin obstruct the lumen (Fig. 4).

Dermis: Frequently there seems to be a definite zone immediately beneath the epidermis in which capillary vessels are dilated and the supporting fibrous tissue is loose in texture (Fig. 2). Sometimes this is accompanied by a scattered infiltration of lymphocytes and leukocytes. In the deep portions of the dermis, inflammatory exudate tends to be grouped principally around the accessory glandular structures and their ducts. In such areas the infiltration is relatively compact and surrounds in cuff-fashion a network of small blood vessels and lymphatics (Figs. 5 and 6). Endothelial proliferation is commonly observed in these blood vessels, particularly in those of capillary size. The degree of this process is variable but sometimes actually may almost occlude the vascular lumen. Thrombosis of small vessels may be observed and attempts at recanalization are evident (Fig. 7). Hyperplastic and occlusive alterations are notable in the small blood vessels surrounding the coils of the apocrine glands. Small branches of nerves are sometimes involved but show no characteristic alterations.

The inflammatory foci tend to be embedded in dense collagenous tissue so that the low-power view shows alternating foci of cellularity and fibrosis. The nature of the exudate is variable between specimens and between foci in the same specimen. Lymphocytes and large monocytes predominate, and polynuclear leukocytes are

seen, mostly in small necrotic foci, but also infiltrating the epithelial layers, both in the glands (Fig. 12) and the epidermis (Fig. 3). (Table I).

Apocrine Glands: Exudation is seen surrounding the coils of the apocrine glands, accompanied by varying degrees of fibrosis (Fig. 8). Variable degrees of vacuolization and degeneration are found in the epithelium of the apocrine glands (Figs. 8 and 9). Sometimes cells have lost their nuclei, and adjacent cells occasionally show evidences of swelling and multiple nuclei (Fig. 12). Some of the alterations in the apocrine glands are of striking degree. The epithelium is fusiform and the lumen reduced to a crevice, but normal myoepithelium is still present (Fig. 10). Cystic dilatation of some tubules of an apocrine lobule is often found and is characterized by the irregularity and regressive alteration of the epithelial lining cells (Fig. 11). The ducts of the apocrine glands are often embedded in dense fibrous tissue. Peri- and intra-ductal infiltration of leukocytes sometimes occurs (Fig. 5). Evidence of obstruction to the outflow of glandular secretion is rarely detected in these sections, although the orifices of the ducts seem in many instances to be reduced through the presence of plugs.

TABLE I.
PERCENTAGE AND TYPE OF LEUKOCYTES
IN DERMAL EXUDATE.

(Based on 1000 cells in 10 cases)

TYPES	PER CENT
Lymphocyte	66
Monocyte	14
Plasma Cell	10
Neutrophil	8
Eosinophil	1
Questionable	1

Sebaceous Glands: The sebaceous glands in these specimens are relatively unaffected. The increased amount of fibrous tissue and vascular engorgement in the superficial part of the cutis rarely seems to cause any alteration in size or shape of the sebaceous glands. No evidence of secretory obstruction is present nor any tendency toward adenomatous hyperplasia.

DISCUSSION

In chronic otitis media and mastoiditis the external canal usually does not show gross evidence of suppurative inflammation on superficial inspection, and the presence of pronounced inflammatory changes in its epithelium has not been recognized as a regular concomitant finding. Upon microscopic examination, however, all of the 40 specimens of the external auditory canal removed during the performance of radical mastoidectomies revealed the characteristics of chronic inflammatory changes described above.

At least two pathways could be involved in the extension of bacterial invaders from the middle ear or mastoid process to the external meatal wall: 1) vascular-lymphatic diffusion from the middle ear to the deep layers of the skin of the ear canal, and 2) penetration of the epidermis from the lumen of the external auditory canal. The findings in this study tend to support the former hypothesis in that the reaction is vascular and perivascular and the deep layers show the greatest degree of exudation. It is not impossible, however, that this might also occur in an inflammatory process of the skin of sufficiently long standing, although primarily derived from a surface infection which penetrated the deeper layer.

It is noteworthy that the apocrine glands suffer more damage as the result of the chronic inflammatory process than do other structures. This seems to be at least partly explicable by their anatomic situation in the deeper part of the dermis and their relative confinement by the cartilaginous ring. Tissue pressure is more apt, therefore, to alter adversely the apocrine glands than the sebaceous glands, which are situated superficially. Second, a close relationship of the vascular engorgement and inflammatory exudation to the apocrine glands has been regularly observed. This seems to be a natural result of the anatomic distribution of the small vessels which arise from a network existing just inside the perichondrium. In their perpendicular course toward the surface the vessels are in close contact with the coils of the apocrine glands. In all of the cases here described, considerable active inflammation accompanied by cellular exudation was still present. In the later stages of inflammation vascular obliteration occurs and, coupled with the development of fibrous tissue, is probably responsible for the severe shrinkage and degeneration of portions of the secretory structures of the apocrine glands.

SUMMARY

Serial sections of the skin of the external auditory canal were obtained from 40 patients with chronic otitis media and mastoiditis. Hyperkeratosis, inter- and intracellular edema, and plugging of the

duct orifices were observed. In the dermis pronounced edema, cellular infiltration, vascular hyperplasia, and obliteration were present. Inflammation, degeneration, and necrosis of apocrine glands were frequently seen.

Present evidence suggests that these inflammatory changes extend by way of vascular and lymphatic pathways from the primary focus in the middle ear or mastoid to the skin of the external auditory canal.

The authors are indebted to Dr. Theo. Walsh for many of the skin specimens and to Dr. M. Giampedraglia, Vernon Fisher, Verna Alford, Mrs. Marjorie Adler and Charles Carr for their technical assistance.

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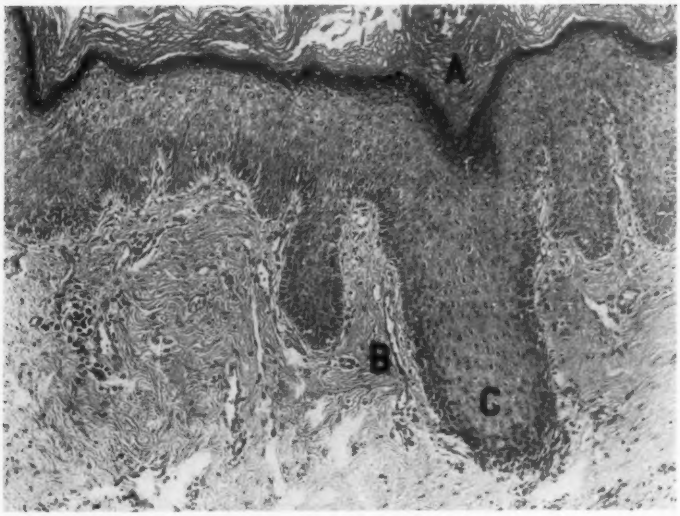

Fig. 1.—Skin of external auditory canal (x 200). *A*, hyperkeratosis; *B*, superficial dilated vessels; *C*, elongated epidermal peg.

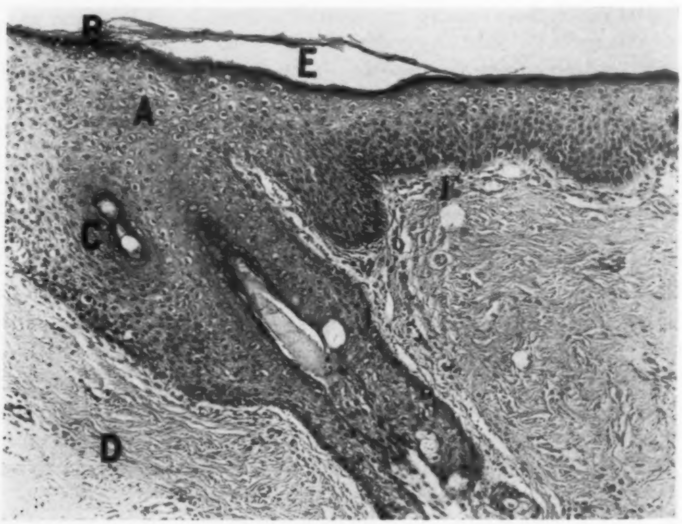

Fig. 2.—Skin of external auditory canal (x 200). *A*, intracellular edema; *B*, hyperkeratosis; *E*, intracorneal space; *C*, plugged intraepidermal duct; *F*, superficial edematous layer; *D*, dermis.

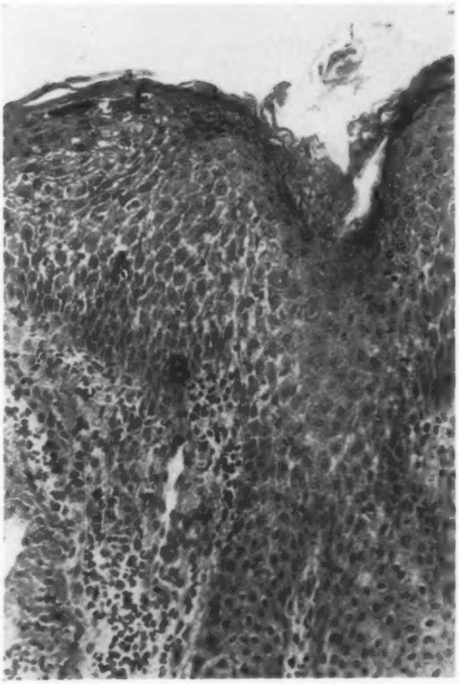

Fig. 3.—Skin of external auditory canal showing intercellular edema and leukocytes infiltrating the epidermis. *A*, intercellular edema; *B*, infiltrating leukocytes; *E*, parakeratosis.

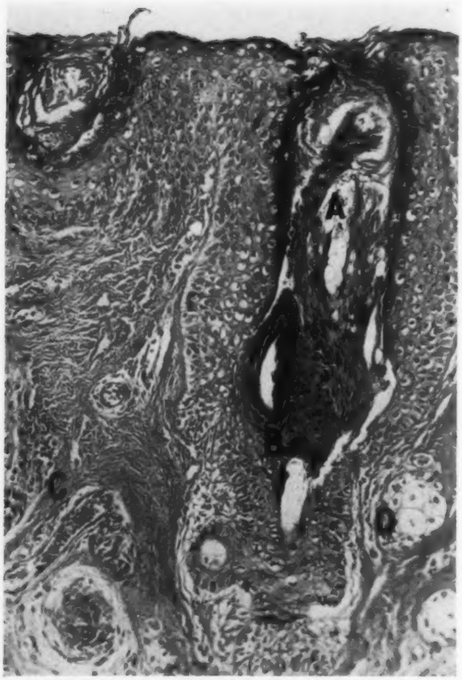

Fig. 4.—Skin of external auditory canal showing keratin plug in pilosebaceous unit. *A*, keratin plug; *B*, pilosebaceous unit; *D*, sebaceous gland; *C*, engorged capillary.

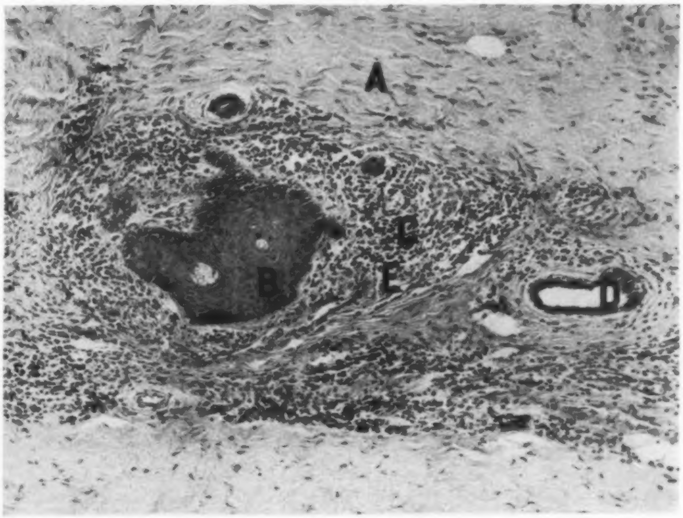

Fig. 5.—Cross-section of dermis showing perifollicular cellular infiltrate. *A*, fibrosis; *B*, section thru hair follicle; *C*, cellular infiltrate; *E*, dilated and hyperplastic capillary vessels; *D*, duct of an apocrine gland.

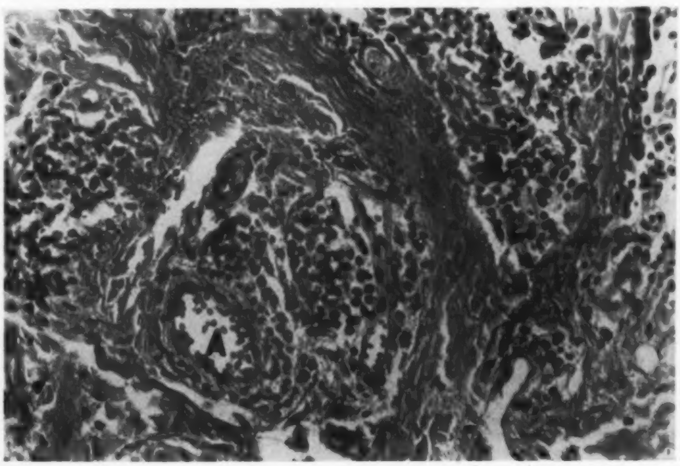

Fig. 6.—Skin of external auditory canal showing perivascular infiltrate. *A*, capillary; *B*, focal infiltration of lymphocyates; *C*, perivascular lymphocytes.

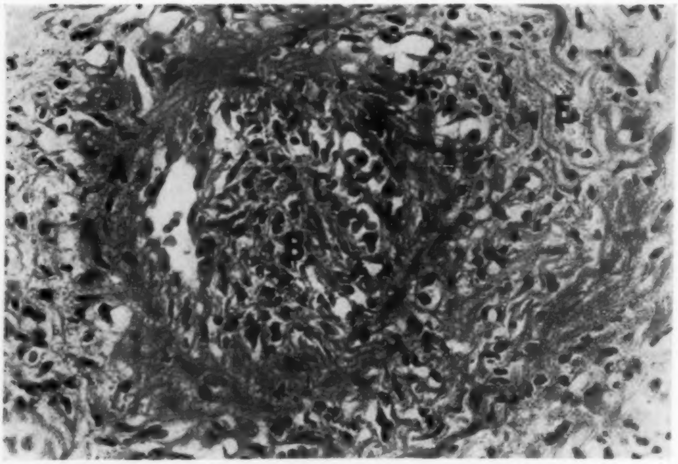

Fig. 7.—Skin of external auditory canal with thrombosed vessel showing recanalization. *A*, vessel wall showing endothelial proliferation; *B*, thrombus; *C*, recanalization; *E*, perivascular edema.

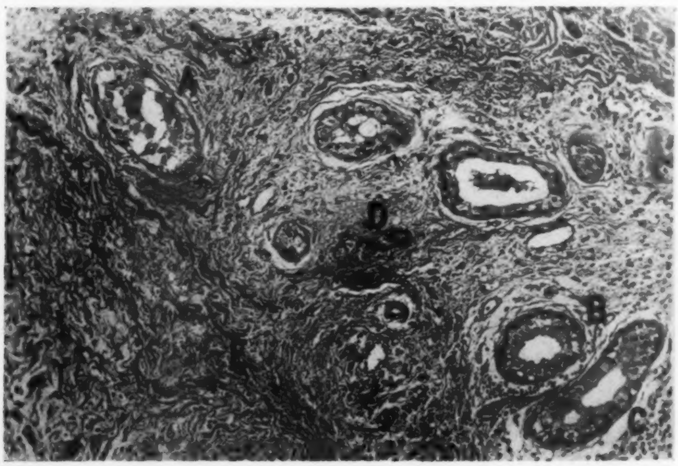

Fig. 8.—Skin of external auditory canal showing vacuolization and various stages of destruction of apocrine glands. *A*, degenerated apocrine gland; *B*, vacuolization of glands; *C*, periglandular infiltrate; *D*, hyperplastic and partly occluded vessel; *E*, fibrosis.

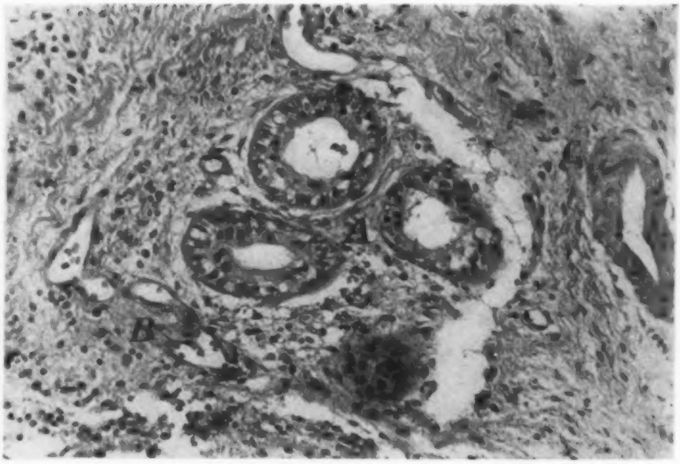

Fig. 9.—Skin of external auditory canal showing vacuolization of epithelium of apocrine glands, dilatation of surrounding blood vessels, and slight periglandular infiltrate. *A*, vacuolated apocrine glands; *B*, dilated capillaries; *C*, thickened wall of blood vessel.

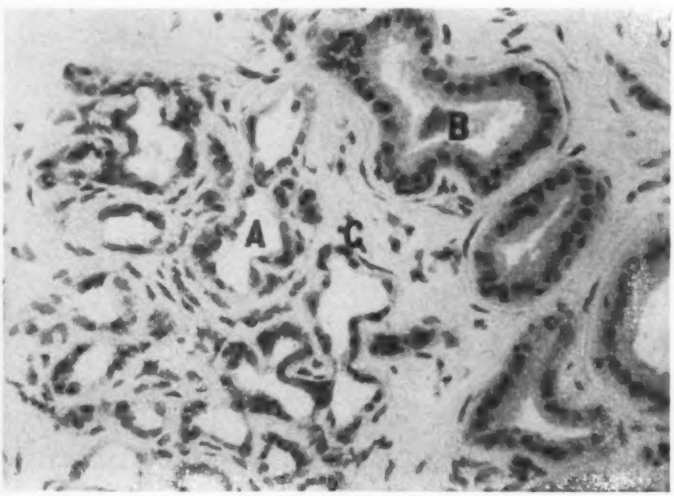

Fig. 10.—Skin of external auditory canal showing atrophy of apocrine glands. *A*, atrophic apocrine gland; *C*, myoepithelial cell; *B*, normal apocrine gland.

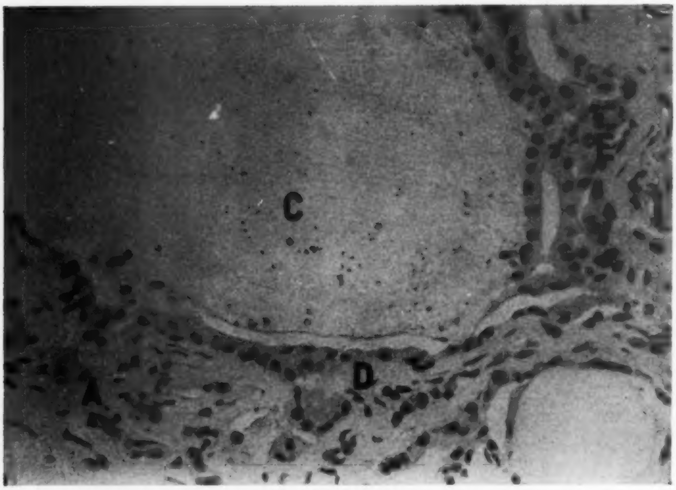

Fig. 11.—Skin of external auditory canal showing cystic apocrine gland. *C*, cystic apocrine gland; *A*, fibrosis; *E*, inflammatory infiltrate; *D*, regressive alteration of epithelium.

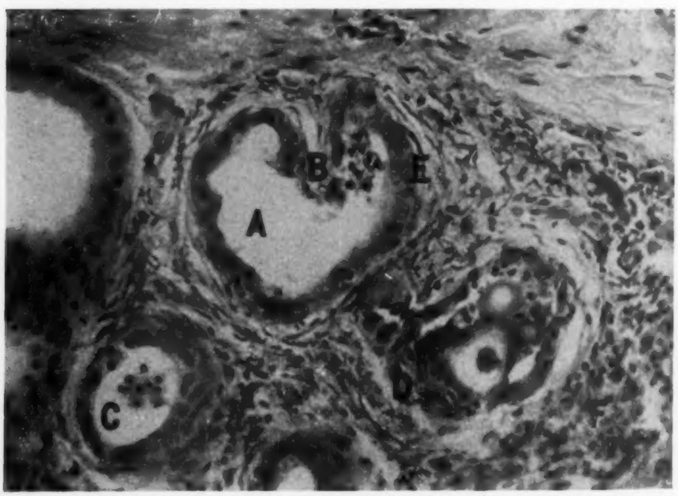

Fig. 12.—Skin of external auditory canal showing intra and periglandular infiltrate. *A*, apocrine gland; *B*, polynuclear neutrophil leukocytes; *E*, epithelial reduplication; *C*, intraglandular exudate; *F*, periglandular cellular infiltrate; *D*, epithelial degeneration.

XXV

VENTRICULOMASTOIDOSTOMY: ITS SIGNIFICANCE TO THE OTOLOGIST

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Ventriculomastoidostomy, introduced by Nosik[1] in 1950, is an operation for the relief of internal hydrocephalus. It is a shunt-type procedure which provides a communication from the lateral ventricle of one side to the mastoid antrum of the same side. References to the procedure are to be found in the neurosurgical, surgical, and pediatric literature;[1, 3, 4] but the writer has been unable to find it described in the otolaryngological literature.

Since the procedure is so intimately concerned with the temporal bone and since the otologist can provide valuable aid to the neurosurgeon in these cases, it is felt that otologists should be familiar with the procedure. The objectives of this paper will be to provide this familiarity and to point out the otologist's importance and responsibilities in providing assistance to the neurosurgeon, this being based on the previous literature and on the experience gained in supplying the otologic assistance at two such operations.

The indication for the operation is internal hydrocephalus of either of the two characteristic types: (1) *communicating,* caused by obstruction beyond the fourth ventricle, overproduction of cerebrospinal fluid, or poor absorption of fluid by blockage of the arachnoid villae, and (2) *noncommunicating,* caused by an obstruction between the lateral ventricles and the foraminae of exit from the fourth ventricle. Through the years numerous operations have been devised to shunt the excess spinal fluid to almost every conceivable part of the body. At present coagulation of the choroid plexus or insertion of a catheter from the lumbar subarachnoid space to the peritoneum or a ureter are the most popular forms of surgical treatments for the communicating type, and Torkildsen's ventriculocisternostomy for the non-communicating type. Ventriculomastoid-

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Presented at the New England Otolaryngological Society Meeting, November 18, 1953.

ostomy is the newest of the shunt-type procedures; and since it is relatively new and unestablished, it is usually reserved for cases which might not tolerate the longer, shunt-type operations or coagulation of the choroid plexus. Since the excess fluid is completely removed from the ventricular circulation, it is immaterial in this operation whether the hydrocephalus be of the communicating or noncommunicating type.

The main objection to the operation at present is the potential danger of meningitis due to ascending infection from the ear. Nosik, however, did not find this a problem in his first series of nine patients, one of whom had survived over two years without complications. One case developed meningitis one month postoperatively, but in this case the drainage was not satisfactory. He postulates that the cilia of the eustachian tube and the directional flow of the cerebrospinal fluid may prevent retrograde infections. Secondary meningitis does represent a real potential danger, however, and until more data is available to indicate that it is not a serious danger, the operation should probably be restricted to adults in whom the incidence of otitis media is less than in children.

Usually the otologist is not too concerned with the type of hydrocephalus or indications since the neurosurgeon has usually decided on the operation before the otologist is consulted. It behooves the otologist to be familiar with the whole subject, however, since the neurosurgeon might be more inclined to use this type of operation if he knows the otologist is familiar with the operation and with the general subject of hydrocephalus. In this connection the reader would do well to consult Jackson's excellent review of the subject.[2]

A complete description of the operation with its results in nine cases is to be found in Nosik's original articles.[1, 3, 4] In general the technique is that of placing a small tube (inside diameter of 1 mm) from the temporal horn of the lateral ventricle through the tegmen antri into the mastoid antrum. This drains off the excess cerebrospinal fluid via the mastoid antrum, middle ear, and eustachian tube to the nasopharynx.

By means of a high postaural incision the neurosurgeon makes a 3 cm round opening in the squamous portion of the temporal bone and elevates the dura to expose the superoanterior surface of the temporal bone.

At this point the otologist enters the picture to make an opening through the tegmen antri into the mastoid antrum. The tubing to be used has been decided on beforehand, usually plastic with a 1

mm inside diameter, and the tegmental opening is made to provide a snug fit. A special tantalum tip is available to hold the tubing in place by means of prongs which are pressed into the bone of the tegmen. In our two cases, rubber tubing was used; and by fashioning the tegmental opening exactly, we found the tantalum tip unnecessary. This opening can be made to fit the tubing exactly in order to prevent leakage. The tegmen antri can be identified by two means: 1) by use of a light placed in the ear canal as described by Nosik, or 2) by familiarity with the anatomy of the temporal bone and the knowledge of the relation of the mastoid antrum to the eminentia arcuata. Its position varies, but usually the antrum lies approximately 1 cm posterior and lateral to the eminentia.

In one of our two cases the Cameron light in the external canal showed up the tegmen antri very nicely, but in the other case the tegmen was thicker and more reliance had to be placed on a knowledge of the anatomical relations in placing the opening.

The other or proximal end of the tubing is now placed in the temporal horn of the lateral ventricle by the neurosurgeon, and the shunt is established. Nosik describes bringing the tube down inferiorly from the ventricle in a straight line. We found it easier to insert the tube into the ventricle through a small opening in the lateral aspect and then to bring it to the mastoid opening along the surface of the temporal lobe. Although this produced bends in the tubing, they were gentle curves and there was no kinking.

Before closing, 1 cc of indigo carmine is injected into the ventricle, and the patency of the shunt checked by observing the appearance of dye in the middle ear. Here, again, the otologist is helpful since he is better trained to pick up the gradual, bluish discoloration of the tympanic membrane as the dye enters the middle ear. Once the patency of the shunt is assured, the wound is sutured in layers.

Aside from his assistance at the operation, the otologist can perform an important function in the preoperative evaluation of the ears and the choice of which ear to use. In this connection a complete examination of the ears is in order. The drum membrane should be intact and preferably normal; but calcification, scarring, and other evidence of old, healed infection is no contraindication. The eustachian tubes should be checked for patency. X-rays of the mastoids should be taken. It is preferable to have a pneumatized mastoid; but a sclerosed mastoid, in the absence of any active infection or history indicating chronic infection, does not preclude the use of the ear. In the case of a sclerosed mastoid, the antrum would

be more difficult to find by the use of a light in the canal; but it should be easily located by its relation to the arcuate eminence. In the event that both ears are suitable by the above criteria and there is a difference in hearing, it would be wise to use the poorer hearing ear. In the postoperative convalescence it is well to give these patients a mild excess of salt in their diet and to test for depletion of electrolytes from the blood secondary to the loss of cerebral spinal fluid through the eustachian tube. However, since this is ordinarily swallowed, no serious reduction in sodium and chloride ions requiring replacement should ensue, as is the case after ureteral shunting.

A discussion of the cases mentioned above (from the Neurosurgical Service, Massachusetts General Hospital) has been purposely omitted since it is beyond the scope of this paper. Suffice it to say that both cases were of the noncommunicating or obstructive type in adult individuals, one due to tumor and the other due to trauma. Both patients were almost moribund at the time of operation. One lived 9½ weeks after the operation and the other 16 days. Both were improved by the procedure; one slightly, one rather markedly. Neither developed meningitis or evidence of recurrent hydrocephalus in the relatively short period after operation.

The author has recently had the opportunity of assisting in a third case. This very interesting patient of Dr. J. C. White was a 30-year-old female from Guatemala whom he saw first in November, 1953, with a history of intermittent nausea, vomiting, dizziness, and headaches for a year and a half. Air studies showed internal hydrocephalus. A posterior fossa craniotomy revealed an inflammatory obstruction at the foramen of Magendi through which a catheter could be passed. To relieve the hydrocephalus a ventricuocisternostomy was done.

The patient was improved by this operation until one month postoperatively when her nausea, vomiting, and headache returned. Air studies at this time (December 6, 1953) showed persistent or recurrent internal hydrocephalus due to obstruction in the fourth ventricle.

On December 7, 1953, a second posterior craniotomy revealed obstruction of the fourth ventricle by a cysticercus cyst (taenia solium). This was removed; and feeling that the obstruction was overcome, the ventriculocisternostomy tube was removed. The patient was markedly improved for five days postoperatively; but by December 12, 1953, her nausea, vomiting, and headache returned and became progressively worse. Air studies on December 30 showed

obstruction at the outlet of the fourth ventricle and massive enlargement of the fourth ventricle.

Due to scarring resulting from her two previous craniotomies, a ventriculomastoidostomy was decided on to relieve her hydrocephalus. This was done on January 2, 1954. The technique was that previously described using a rubber catheter with an inside diameter of 2 mm (No. 8 Fr.) and bringing it down over the surface of the temporal lobe. The use of a light in the ear canal was of no help in localizing the antrum because the mastoid was well pneumatized, and the whole superior surface of the temporal bone transmitted light equally. Here again a knowledge of the anatomy was essential in placing the mastoid opening.

Postoperatively the patient did very well. Her nausea, vomiting, and headaches disappeared; and she was again able to take solids by mouth. Her only complaint was that of a fullness in the ear which had been operated upon. This ear showed the typical picture seen in serous otitis media; and with the nasopharyngoscope, one could observe cerebrospinal fluid coming from the eustachian tube orifice. She was discharged from the hospital 21 days postoperatively and to date (three months) has made an uneventful recovery.

SUMMARY

(1) The technique of ventriculomastoidostomy is presented so that the otologist may be familiar with it.

(2) The importance and responsibilities of the otologist in this operation are discussed.

243 CHARLES STREET.

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XXVI

LETHAL GRANULOMA OF THE MIDLINE FACIAL TISSUES GRANULOMA GANGRAENESCENS

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An unusual type of granuloma has been described as occurring in the face and upper respiratory tract which is progressive, destructive and, in most instances, fatal. The disease has various names, all characterizing the word granuloma: gangrenous, lethal, ulceration, infectious, mutilative, malignant and idiopathic. These give little or no clue to the etiology.

The first case in the literature was that described by P. McBride[1] in 1896. Only a brief description is given but nevertheless, it is sufficient to permit the case to be included in the group. Subsequently, no report is found until 1921 when Woods[2] described a case. Since then, approximately a hundred others have been reported. Joisten[3] in the German literature and Stewart,[4] Hoover,[5] Hargrove,[6] and Williams,[7] in the English and American, have stimulated recent interest in this disease.

ETIOLOGY

It is not known whether the disease is infectious or neoplastic. The majority of investigators favor the former but neither bacteriologists nor mycologists have found an etilogic agent. Repeated animal inoculations and cultures for bacteria, yeasts, fungi and viruses have failed. The usual flora and staphylococci were commonly found. Some authors described fusiform bacilli and spirochetes and believed the lesions to be not unlike Vincent-Plaut's angina.[8]

From the Departments of Pathology (Dr. Breckenridge) and Laryngology and Broncho-Esophagology (Drs. Wagers and Baltzell) Jefferson Medical College, Philadelphia, Pennsylvania.

Several have suggested that the disease was a form of periarteritis nodosa particularly involving the nose.[8, 9, 10] They demonstrated a necrotizing arteritis with eosinophils. The rest of their findings, however, were not compatible with the disease.

Clinicians familiar with gangosa feel certain that the disease under consideration is of this order.[7] Both are characterized by a destructive ganuloma involving the nose and facial tissues. The only differences are the prognosis and the geographic distribution. Gangosa is rarely fatal and occurs only in the West Indies, South Pacific, West Africa and the Belgian Congo.[11]

Others suspect it of being cancerous.[12, 13] They state that the histological structures resemble various forms of sarcoma, or one of the lymphomas. Some of the neoplastic diseases suggested are Hodgkin's sarcoma, reticulum cell sarcoma, mycosis fungoides, and Kaposi's sarcoma.

Bergqvist and Koch[14] envisaged a new tumor, hitherto not described, which was so affected by secondary inflammatory changes that the whole microscopic structure was distorted.[12]

Ewing,[15] in reviewing sections from Wood's case, was of the opinion that the histological appearance most resembled syphilis, though lacking specific qualities. He stated that, unless it was an entirely new disease, we are thrown back on syphilis or mycosis fungoides.

Williams[7] stresses the possibility that it might be the result of hyperimmunity. He believes that the tissues in this area of the nose have an innate capacity to develop hyperimmunity, possibly greater than any other area of the body. He suggested that the profound weakness and lethargy produced in the later stages are caused by dysfunction of the suprarenal cortex and that this may be the underlying cause of the granulomatous reaction. Brozek and Vanek[16] reported two cases which they believe were the result of anaphylactic reactions.

According to Stewart's classical description the course of the disease is divided into three stages based upon the symptoms and the pathological progression.

The prodromal stage, is characterized by intermittent nasal obstruction associated with a postpharyngeal discharge and a watery or serosanguineous rhinorrhea. Occasionally the disease is initiated by a superficial ulcer of the nasal vestibule, nasal septum, or palate. In some instances there is a history of pre-existing infection of the paranasal sinuses. When a submucous resection is performed it is almost

always followed by perforation of the septum and spread of the disease.

The second stage is the period of active disease. It generally lasts from ten to eighteen months. It is characterized by a small, shallow ulcer on the nasal septum, inferior concha, floor of the nose, or palate covered with an inspissated crust which on removal reveals a granular surface resembling granulation tissue. A purulent or sanguinopurulent discharge develops. The lesion frequently has a very fetid odor. It tends to invade the interior of the nose from the roof of the mouth and the face from inside the nose. Early in the involvement of the facial tissues, the nose and paranasal structures become indurated and swollen. As the lesion progresses the palatal, nasal, and malar bones undergo necrosis and sequestration. Abscesses may develop in the soft tissues of the face and mouth. The temperature is normal or slightly elevated. The blood count is either normal or shows a slight leukocytosis or mild leukopenia. The differential blood count is usually normal. Septicemia is uniformly absent. The most striking observation of the second phase is, that despite the apparent gravity of the lesion, the patient enjoys a sense of well-being except for varying degrees of weakness or lassitude.

The third or terminal stage is characterized by exhaustion, and extreme mutilation. The face may be exceedingly disfigured with a large central aperture, and there is the fetid odor of putrefaction. The margins are indurated with rolled, heaped-up tissue. The eyelids may be swollen with a purulent discharge exuding from between the lids. The nasal septum, nasal conchae, and hard and soft palates may be obliterated. Often the lateral walls of the nose are completely eroded baring the piriform aperture and malar bones. The pharynx and larynx may show extensive necrosis or may be covered with a granuloma. In the central area of the face only a portion of the fleshy dorsum of the nose may remain. Even this may disappear together with portions of the eyelids or eyes. Only the tongue and basisphenoid are invariably spared. The remaining exposed surfaces lining the ulcer are covered with a heavy dirty-brown or greenish-brown crust. In most instances there is little oozing through this crust. Recurrent hemorrhage due to erosion of vessels is often troublesome and may cause sudden death. Usually, however, death results from exhaustion and inanition, with terminal temperatures as high as 106 or 107° F. Other causes include, meningitis or brain abscess, septicemia, and pulmonary complications.[19]

Disseminated involvement of the skin has been described by several investigators.[7] In a patient of Moore's[17] skin lesions of the

lupus erythematosus desseminatus type developed on the elbows, hands and feet and were associated with a rheumatoid arthritis of the knees and ankles. In one of Williams'[7] cases the skin lesions suggested histoplasmosis, but cultures and a skin biopsy were negative for tuberculosis, fungi, and bacteria. At autopsy numerous cutaneous abscesses were found from which only Staphylococcus aureus was recovered.

Constant and unaccountable is the complete lack of effective resistance by the defensive mechanism.[18]

Microscopic examination reveals a coagulation type necrosis with or without the formation of granulomas. In most instances the tissue is composed of numerous inflammatory cells in a predominantly loose stroma. The latter may resemble granulation tissue. The cells are mainly lymphocytes, plasma cells and histiocytes. Eosinophils, neutrophils, and multinucleated giant cells may be prominent. The histiocytes are variable in size and shape. They may be epithelioid in nature and may be vacuolated or contain detritus. The latter may be mistaken for specific inclusions. Reticulum cells are sometimes evident.

The inflammatory cells may conglomerate to form granulomas. The lesion, however, is not characteristic of tuberculosis, Boeck's sarcoid, syphilis, or leprosy. The granulomas may be either of the solid or the necrotic type. These masses are most prominent around vessels and mucous glands. The arteriolar walls frequently show degeneration.

At necropsy there is usually evidence of systemic spread of the process. Aside from the nasopharynx the larynx, trachea, and lungs are most commonly involved. Other organs are the skin, spleen, liver, kidneys, lymph nodes, intestines, adrenal glands, and the middle ear. The metastases are granulomas similar to the primary lesions.

The disease occurs rarely in the first and second decades of life. Only two cases have been reported in children. The ratio of male to female is 20:1.[18]

DIAGNOSIS

The diagnosis is one of exclusion. The disease must be suspected in patients who develop a chronic, progressive and destructive ulcer of the nose or palate which fails to respond to local treatment, antibiotics and chemotherapy.

The failure to find a specific etiologic agent by culture, serologic studies and agglutination tests leads to biopsy, which reveals a nonspecific granuloma. Special stains for tubercle bacilli and B. leprae,

fungus, and yeast are negative. Negative animal inoculations and normal findings in all other laboratory tests are characteristic.

Roentgenograms of the skull during the second and terminal phases may reveal destruction of the bony parts of the nose and sinuses as well as sinusitis. Occasionally the granuloma appears as a bone-destroying tumor.

The disease can remain undiagnosed until necropsy. The mutilation of the face and sinuses alone are typical at autopsy. The dissemination of the disease is more misleading than helpful in arriving at a diagnosis. Undoubtedly cases have gone undiagnosed.

The differential diagnosis must include the specific granulomas, parasitic infections, neoplasms and metabolic diseases. The first group includes syphilis, tuberculosis, Boeck's sarcoid, leprosy, fungous infections (particularly histoplasmosis) glanders, chronic tularemia, anthrax, rhinoscleroma and yaws. These must be excluded by the history, physical findings, duration and progress of the disease, and by laboratory studies. The latter should include cultures for tubercle bacilli, fungi, and aerobic and anaerobic bacteria. Negative findings should be confirmed by animal inoculation. Serologic tests for typhoid, tularemia and undulant fever should also be tried. Biopsies from early lesions are the most revealing. This is particularly true in case of histoplasmosis and scleroma.

Myiasis and leishmaniasis are the only two parasitic diseases to be considered in the differential diagnosis. Myiasis is rather easy to rule out by careful inspection. Naso-oral leishmaniasis, on the other hand, may be difficult or impossible to exclude completely. In certain parts of the tropics this parasite can produce early destruction of the nasal septum, flattening of the nose and necrosis of the alae nasi just as it occurs in syphilis, leprosy, yaws, and lethal granuloma of the midline facial tissues. Unfortunately in the late stages of naso-oral leishmaniasis the leishmania are found only in very small numbers, or they may be absent.

The lymphomas are one group of neoplasms from which it is the most difficult to differentiate lethal granuloma. Exclusion must be based upon biopsy of the face lesions and on lesions which develop elsewhere. Early dissemination with involvement of skin, lymph nodes, spleen, liver, or bone marrow would suggest one of the lymphomas.

Diabetic gangrene is probably the only metabolic disease which need be considered in the differential diagnosis. This should give the careful observer little difficulty in exclusion.

In the Plummer-Vinson syndrome certain changes occur in the nose but these are atrophic rather than destructive. In addition the syndrome is intimately associated with a severe anemia, particularly of the pernicious variety.

Pemphigus may have its first manifestations in the nose and pharyngeal mucosa in the form of vesicles, necrotic areas, and ulcerations. The Macht-Pell phytotoxin test will be of diagnostic aid in cases of suspected pemphigus.

In erythema multiforme in the upper respiratory tract areas of deformity, atrophy and fibrosis may be the characteristic findings. The common papular lesion is characteristic when it forms the "iris" lesion by peripheral extension and central clearing. The histologic appearance is of value.

Cases of agranulocytosis may be characterized by violent infections, inflammatory exudations, ulceration and necrosis, followed by hemorrhage, and foul-smelling putrefactive nasal discharge. The blood count or the bone marrow aspiration will establish the diagnosis.

Vincent's angina likewise may affect the nasopharynx. Finding of the fusiform bacilli and spirilla in direct smears are diagnostic.

TREATMENT

All forms of therapy have been attempted including local applications, parenteral drugs, heavy metals, antibiotics,[22, 23] and surgical excision.[24, 25] None has been found to be specific and most have failed to stop the progression of the disease. Radium and roentgen therapy have produced, in some instances, resorption of the infiltrations and healing of the ulcers.[10]

Recently cortisone and ACTH have given some encouraging results.[18] Several of the reported recoveries were believed to have resulted from their use.[24, 26] However, not all of the patients treated with one of the corticoids have recovered.

PROGNOSIS

The prognosis is grave. Until 1941 only four patients had recovered.[21] Two had been treated with radium and x-ray irradiation and one was believed to have recovered spontaneously. The other case was atypical.

Since 1941 there have been a few instances of recovery. The follow-up period on some of these patients, however, has been too short to classify them as cures.

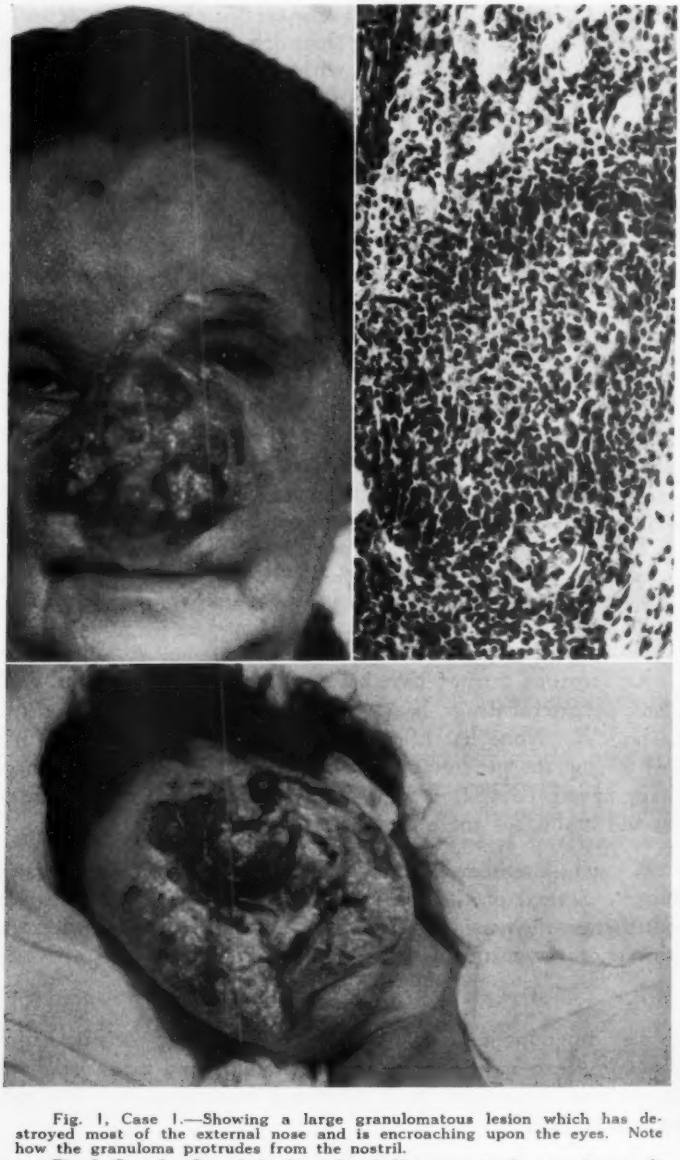

Fig. 1, Case 1.—Showing a large granulomatous lesion which has destroyed most of the external nose and is encroaching upon the eyes. Note how the granuloma protrudes from the nostril.

Fig. 2, Case 1.—One of the few tubercle-like areas in the granulomas. It is composed of epithelioid cells, plasma cells, neutrophils and eosinophils. X200.

Fig. 3, Case 1.—The face is almost completely destroyed. Note the typical absence of involvement of the tongue. Photo taken 10 days before death. (Courtesy of Dr. Edward J. Mazur, Camden, N. J.)

The disease tends to periods of quiescence and, rarely, there is spontaneous recovery. The majority of patients becomes progressively worse and die between four to six years after the onset.

REPORT OF CASES

CASE 1.—A. C., a 61-year-old Italian housewife was first admitted to Jefferson Hospital on June 13, 1949. The chief complaint was an ulcerating lesion of the nose. Apparently she was well until 19 years before admission when, during a pregnancy, she developed asymptomatic, red, non-elevated spots on her cheeks, forearms, trunk, and thighs. The eruption faded with only minor recurrences.

In 1943 a severe sunburn was followed by the development of red pimples on her nose and cheeks and a swelling of her neck. Both gold and x-ray therapy were used. Except for the neck the lesion cleared after 15 months.

A biopsy from the face at that time was reported as "chronic inflammation with sarcoid or tuberculoid changes (leukemia cutis)." She was given further x-ray therapy to the face and injections of bismuth during the next two years. Apparently the nose had become raw towards the end of this period.

In 1947 the lesion of the nose began to progress. A biopsy was diagnosed by a dermatologist as lupus erythematosis. He instituted vitamin E therapy without effect. A fourth biopsy was reported as syphilis or tuberculosis. The serologic tests for syphilis were negative. Calciferol also proved ineffectual.

On her first admission to Jefferson Hospital she had a large, ulcerating granuloma involving the entire dorsum of the nose, the right eye and part of the left (Fig. 1). The conjunctiva of the left eye was inflamed and wept continuously. There were several small scaling, non-ulcerated lesions scattered over the shoulder, thigh, left breast, and neck. Multiple specimens were taken for guinea pig inoculation and histologic study. The guinea pigs failed to develop any specific lesions. The biopsies showed marked acanthosis and dyskeratosis almost to the point of resembling carcinoma. The corium was heavily infiltrated with all types of inflammatory cells particularly eosinophils, plasma cells, neutrophils, and a few lymphocytes. Rarely a tubercle-like area was noted (Fig. 2). They were composed of epithelioid cells, neutrophils and eosinophils and were surrounded by many neutrophils. The tubercles showed no evidence of necrosis. At the time the clinical diagnosis of lupus vulgaris was considered.

Again the serologic tests for syphilis were negative, spinal fluid was not remarkable, and the chest x-rays were normal. The blood

count revealed a leukopenia of 3,600 white blood cells with 18 per cent eosinophils. The urinalysis was negative. Cultures of the lesion were negative for bacteria, tubercle bacilli, and fungi.

A therapeutic test for syphilis was given without any effect. She failed to develop a Herxheimer reaction.

After a review of all the biopsies, a prominent dermatologist of Philadelphia believed the patient had mycosis fungoides. Several series of nitrogen mustard, sodium silicate, hepbisul and ACTH were ineffective.

By June 1950 roentgenograms of the skull showed destruction of the frontal bone and involvement of the sinus with a question of intraorbital involvement.

The patient was cared for at home following her last discharge from the hospital in February 1951. She became a difficult nursing problem and had to be fed liquid food only. The lesion progressed to destroy the entire face (Fig. 3). At the time of death on August 11, 1951 there were no lesions elsewhere that could be determined. A necropsy was not obtained.

Case 2.—J. Z., a 56-year-old merchant seaman was admitted to Jefferson Hospital on September 22, 1949. The chief complaint was of an ulcer on the roof of his mouth of seven months' duration.

In 1942 the patient developed a swelling on the left side of the palate which was incised and which healed after one month. Seven months before admission another lump had appeared at about the same place. It had again been incised, but this time it did not heal. The lesion became ulcerated, gradually increased in size, and discharged a yellowish foul material with a very fetid odor. It did not bleed and was not painful until two months before admission.

During the months just prior to admission, he had anorexia, with a 17 pound weight loss, and tinnitus in the right ear with some enlargement of the cervical lymph nodes.

The patient had immigrated from Greece in 1941. Except for a period of two months in Florida, he had lived in Pennsylvania. In 1912 he was treated for syphilis with "606." In 1935 he had gonorrheal arthritis, in 1944 a hemorrhoidectomy, in 1945 herpes zoster, in 1946 a rectal fistulectomy; and in 1947 sinusitis for which he had had three radium treatments.

He was a well-developed and well-nourished white, middle-aged man not acutely ill. The temperature, pulse, and respiration were

normal. The blood pressure was 104/60. The skin was normal except for intradermal soft nodules on the forearms. The eyes including the fundi were normal. The right eardrum was red and inflamed. There was a necrotizing ulceration of the hard and soft palate with red edges, yellow discharge and apparently on opening into the nasal cavity (Fig. 4). His breath was foul. Pea-sized lymph nodes were present in the cervical chain. Coarse breath sounds with râles were noted at the right base. The heart was normal in size, rate and rhythm. The prostate gland was slightly enlarged.

Initially, and at intervals over the next two years, blood counts, urinalyses, blood sugar, cholesterol, proteins, calcium, phosphorus, phosphatase, urea nitrogen, liver function studies, spinal fluid, electrocardiogram, and serologic tests for syphilis were normal. Sedimentation rate was 18 to 25 mm. P.P.D. was positive in the second strength. Repeated cultures for acid fast bacilli and fungus were negative except for C. albicans. The urine was negative for Bence-Jones protein. The urea clearance was 54 per cent. Biopsies revealed a granulomatous lesion composed of numerous histiocytes, plasma cells and lymphocytes in a loose stroma. Tubercle formation was absent. Cultures of the tissue failed to reveal an etiologic agent.

Roentgenograms of the chest were negative except for a Ghon complex in the right apex. There was demineralization of the sella turcica, and thickening of the maxillary sinus membrane, especially on the left.

After "sopronol" and a course of penicillin, the ulcer improved briefly at first, but then began a slow but relentless extension until the time of death two and one-half years later (Fig. 5). Treatment included Chloramphenicol,® Aureomycin® and potassium iodide, which brought no relief in May and June 1950; nitrogen mustard in August 1950, which gave some relief from pain but had no other effect; bacillomycin in October 1950, which caused such severe local and systemic reaction that it had to be stopped; mapharsen in November 1950, which was stopped because of a fall in blood pressure; antabuse in December 1950, which was followed by purpura; permanent gastrostomy in January 1951, because of a painful oral lesion; ethylparasept in May 1951; local chloresium and acriflavine; roentgen therapy to the area, which did not help; atabrine in October 1951, with no changes noted; stilbamidine, and promin, both without relief.

In March 1951 a red, tender induration had appeared just below the left malar emminence. X-ray showed destruction of part of the lateral sinus wall and part of the inferior wall of the left orbit. X-ray




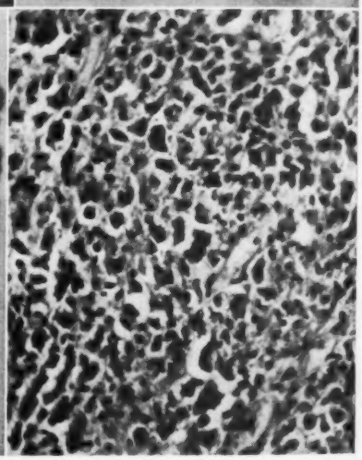

Fig. 4, Case 2.—A necrotizing ulceration of the hard and soft palate with red edges, a yellow discharge, and apparently on opening into the nasal cavity.

Fig. 5, Case 2.—Shows progressive destruction of the soft and hard palate. Note the uvula is hanging by a narrow bridge of soft tissue on either side. The lesion had a very fetid odor.

Fig. 6, Case 2.—A few weeks before death. The swelling represents involvement of the left maxillary sinus with fistulas and sinuses between the skin, sinus, nose, and mouth.

Fig. 7, Case 2.—The granuloma is composed of large, irregular histiocytes together with lymphocytes, fibroblasts, and epithelioid-like cells. A number of the histiocytes contain dertitus. Some of the inclusions vaguely suggested the inclusion bodies of Histoplasma capsulatum. X200.

treatment to the area did not help and subsequently a sinus opened up in the indurated area just below the left malar eminence. At this time a muscle biopsy, laryngeal examination and numerous cultures for fungus were negative.

Several x-ray examinations of the chest were negative until November 27, 1951 when a homogeneous, round extradensity was observed in the right lower lung field with increased bronchial markings between it and the hilum. A second extradensity of the lung became evident on December 26th higher in the right lung. By mid-January both masses had increased in size. Bronchoscopy was negative on two occasions and bronchial secretions were negative for neoplastic cells and fungus.

The patient developed a progressive anemia and cough. The cough was productive of bright red blood. On February 11, 1952 the patient had a massive hemoptysis and died.

For several months prior to death the patient required narcotics for severe facial pain. The lesion became so offensive that he had to be kept in isolation. At the time of death two sinuses were present on the face and a third just below the left orbit (Feb. 6).

At autopsy the granuloma had produced diffuse destruction of the soft palate, posterior portion of the hard palate, left maxilla, floor of the left orbit and bones of the nose. An infiltrating granuloma with multiple abscesses was present in the right lower lobe of the lung. A ragged end of a medium-sized vessel projected into the largest abscess. Histologically the granulomatous areas were composed of large, irregular cells together with lymphocytes, fibroblasts, and cells resembling epithelioid cells (Fig. 7). The large cells were probably histiocytes for some of them contained nuclear detritus. A few of the cells were in mitosis. Others resembled reticulum cells. The inclusions seen in the histiocytes were believed to be bodies resembling Histoplasma capsulatum. They were not typical, however, and the cultures after six weeks were negative.

Case 3.—J. D., a 32-year-old white bookkeeper born in Pennsylvania was first seen at Jefferson Hospital on September 26, 1949. The chief complaint was hoarseness and occasional dyspnea. He had had some sinus trouble in June and had also had all his upper teeth removed for pyorrhea. He gave no history of syphilis or injury to the nose. Both his parents had tuberculosis.

Physical examination revealed absence of the nasal septum except for the extreme anterior portion. The roof of the nasal cavity was

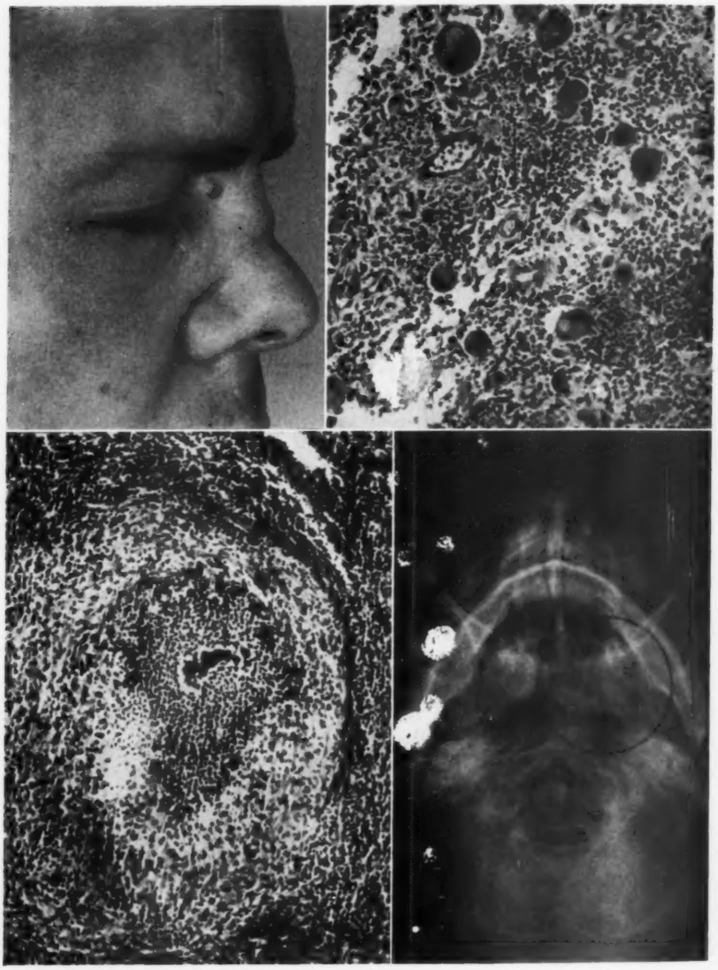

Fig. 8, Case 3.—Shows a small fistula on the inner aspect of the infra orbital area. Note the saddle nose which has been described in a number of cases. (Courtesy of Dr. F. J. Putney, Philadelphia, Pa.)

Fig. 9, Case 3.—Shows granulation tissue containing multinucleated giant cells and focal collections of neutrophils and plasma cells, particularly around blood vessels. X100.

Fig. 10, Case 4.—Shows one of many tubercles composed of epithelioid cells peripherally, and neutrophils centrally. This one contains an amorphous mass in the center. Special stains did not assist in the identification of this mass. X100.

Fig. 11, Case 4.—An x-ray of the base of the skull showing a soft tissue mass destroying the petrous portion of the left temporal bone and extending into the foramen lacerum.

covered with crusts. The pharynx was slightly inflamed. There was a swelling bilaterally in the subglottic region.

X-ray examination of the chest was negative. The serologic tests for syphilis were negative. Cultures of the nose were negative for acid-fast bacilli and fungus. The skin test and complement fixation for histoplasmosis were negative.

In March 1951 he was admitted for emergency tracheotomy because of marked stenosis. The primary lesion had continued to destroy the middle turbinate, the ethmoid region and ethmoid cells and a portion of the inferior turbinates bilaterally. There was a large amount of pus and crusting. A small fistula had formed on the inner aspect of the right infra-orbital area (Fig. 8). X-ray examination of the paranasal sinuses showed unusually extensive involvement of the ethmoid cells. The sphenoid and frontal sinuses were reduced in radiotranslucency, and there was some loss of margination of the frontal sinus with replacement with a sclerosing osteitis. A similar osteitis had occurred around the corresponding maxillary sinuses. A biopsy showed granulation tissue containing numerous multinucleated giant cells and focal collections of neutrophils and plasma cells (Fig. 9). In other areas these same cells were scattered in the edematous stroma. The surface epithelium was completely ulcerated.

On January 28, 1952 the nasal lesion showed improvement with replacement of the crusts with scar tissue. The laryngeal lesion continued to progress. The lumen was the size of a pinhead and the patient became aphonic. The fistula on the inner canthus continued to drain. The lesion was about the same in June 1952 when last seen.

Case 4.—C. D., a 58-year-old white Pennsylvania farmer was first admitted to Jefferson Hospital on January 15, 1947. The chief complaints were of deafness, nasal obstruction and pressure on the left side of the face. Examination revealed slight retraction of the eardrum. The left antrum was clouded on transillumination. The nasal septum deviated to the right. A tumor, the size of a marble, arose from the floor of the left choana which obstructed the left eustachian tube. It was covered with mucosa except for a few small, yellow elevations scattered over the surface.

The bulk of the mass was removed with a snare. The cut surface was composed of several round chalky white, slightly moist nodules measuring up to 8 mm surrounded by soft, tan tissue. Histologically it was composed of lymphoid tissue containing granu-

lomas. The granulomas were made up of epithelioid cells peripherally and neutrophils centrally. A few of them contained an irregular amorphous, purple mass in the center of the granuloma (Fig. 10). Special stains were unrevealing.

Laboratory studies were negative. They included: Serologic tests for syphilis, febrile agglutinations (including tularensis), Frei test, sedimentation rate, cultures directly and from tissue for bacteria, fungi, and tubercle bacilli, animal inoculation (mice and guinea pigs), complement fixation test for Histoplasam capsulatum, and dark field examination. X-rays of the chest were negative and those of the sinuses showed slight clouding of the ethmoids.

When the patient was seen on April 22, 1953 with the same symptoms, the lesion now involved the oral surface of the soft palate on the left side and the left lateral wall of the posterior nasal space. It was ulcerated and firm. Similar small, yellow nodules also extended across the nasal surface to the right lateral pharyngeal wall. A biopsy of the lesion was again done and all the studies repeated. Histologically the granuloma was similar to the first. All the studies were negative. He was given antibiotics of various types but failed to respond. When last seen on December 10, 1953 the granuloma was twice its original size and filled both posterior choanae.

Biopsy and laboratory studies were similar to the former ones. An x-ray of the skull now showed erosion particularly of the petrous portion of the temporal bone in the area of the foramen lacerum (Fig. 11). The patient was discharged, unimproved, to be followed periodically.

Case 5.—P. P., a 20-year-old white female typist was admitted to Jefferson Hospital for the fourth time on April 5, 1950. She complained of nasal obstruction with a purulent and sanguineous discharge for the previous five years. Hoarseness had been present for the past three months and tinnitus, deafness, and cough had recently developed. The previous admissions were for septicemia in 1942, splenectomy for congenital hemolytic anemia in 1943, and an unexplained petechial rash of the ankles in 1949.

Examination of the nose revealed a large amount of clotted blood mixed with purulent secretions on both sides of the nose. The septum deviated to the right and the mucosa was superficially ulcerated. The vault of the nose, middle turbinate and ethmoid area on the left were replaced by a firm mass. The pharynx exhibited some granulomatous changes with prominent lymph follicles. Similar lesions with crusts were noted on the vocal cords. The sinuses did

not transilluminate. The rest of the physical examination was not revealing except for the splenectomy scar and numerous small scars about the ankles.

A biopsy specimen of the mass in the nose was composed mainly of a loose stroma containing many reticulum cells and histiocytes. A moderate number of eosinophils and occasional plasma cells and lymphocytes were noted. It was believed to be a non-specific granuloma. Except for a slight leukocytosis, the laboratory studies were normal. Serologic tests for syphilis were negative. Cultures from the nose were positive for Candida albicans only. Skin tests with blastomycin, histoplasmin, and tuberculin antigen were negative. Treatment consisted of x-ray therapy.

On April 13, 1950 the patient was readmitted because of a two week history of diarrhea and eruption over the skin and mouth. She was acutely ill and had a fever of 102° F, a pulse of 120 and tenderness in the right upper quadrant. The mouth lesions were white, flat placques surrounded by a red mucosa. A diagnosis of cholecystitis with cholelithiasis was made and cholecystectomy performed. The pathologic diagnosis was acute cholecystitis superimposed on a chronic cholecystitis with cholelithiasis. She made an uneventful recovery and was discharged.

When last seen in October 1953 the lesions of the nasopharynx had not progressed.

COMMENT

In the five cases described here, an infiltration in the skin of the face, nose, or palate gradually developed in otherwise healthy individuals. This slowly increased in extent, involved tissue deeper down, produced necrosis, and gave rise to deep defects in the soft tissues and the corresponding parts of the skeleton. Two of the patients died in a state of cachexia. The lesions in the other patients continue to be destructive and progressive. All of the cases are essentially similar to those earlier described under the designation of "lethal granuloma of the mid-line facial tissues," "granuloma gangraenescens," "malignant granuloma," and "osteomyelitis necroticans facieri."

As a group no clue has yet been discovered to establish the etiology.

The first case was diagnosed as mycosis fungoides by one of the leading dermatologists in the country. The biopsies were confirmed by others. Yet when she died, clinically the disease was limited to the face. This does not rule out the possibility of mycosis fungoides

particularly when no autopsy was performed. Yet it is unusual that her skin lesions over the trunk and extremities should disappear. None of the other cases herein reported suggested mycosis fungoides.

The second case was believed to have been systemic histoplasmosis. Yet repeated biopsies and numerous cultures failed to reveal Histoplasma capsulatum. Because Candida albicans was repeatedly recovered on most of the cultures, it was felt that this fungus overgrew the culture media and thereby prevented the Histoplasam capsulatum from growing. But surely if it had been histoplasmosis, the organisms would have been positively demonstrated in tissue or in culture at one time or another. The limitation of the findings at necropsy to the respiratory tract and the absence of involvement of the adrenal glands are against this having been histoplasmosis.

It was at first planned not to report the last three cases because the patients are all living. For that reason, however, this group is more important to us. By periodic examination, with repeated laboratory studies, biopsies, cultures, and therapeutic tests, they may help us uncover one of the many facets of this mysterious disease.

SUMMARY

Five cases of lethal granulomas of the mid-line facial tissue are described. Two of the five patients died; clinically one was believed to have had mycosis fungoides, the other suggested systemic histoplasmosis. The three living patients are being followed periodically in an attempt to learn more about the disease.

JEFFERSON HOSPITAL.

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XXVII

HEMOPTYSIS

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The problem of hemoptysis is one which commands a major share of consideration in the proper evaluation of pulmonary diseases. It is one of the signs which must be carefully evaluated and its source accurately identified in order to establish the correct diagnosis. In many instances it is the first omen to the patient that all is not well. The spitting of blood does not in itself incriminate the lung, but does point the finger of suspicion directly at it. Bleeding which arises from the nose, nasopharynx, sinuses, mouth, teeth, tongue, hypopharynx, larynx, esophagus, or stomach and, in rare instances, the small bowel, may cause the expectoration of bright blood in such quantities as to be disturbing to the patient. All of these other sources of bleeding must be carefully examined and eliminated before the bleeding may be diagnosed as hemoptysis and before definitive treatment of the pulmonary pathological condition may be begun.

Endoscopy in the study of hemoptysis is but one of the diagnostic methods available.

The amount of bleeding does not, of necessity, give any index as to the underlying pathology. In the case of daily bleeding which recurs regularly for days or weeks one should be suspicious of malignancy.

In pulmonary tuberculosis 60 per cent to 80 per cent of the patients have hemoptyses,[1] and the bleeding is episodic (recurring at varying intervals) and is of three distinct types. The first type is mild and is the most common form. It usually arises from tuberculous ulcerations of the bronchial mucosa which are common indeed. This is a form of hemorrhage arising from the smaller branches of the bronchial artery. It is not common for granulation tissue within a tuberculous cavity to produce bleeding because of the extensive fibrosis and scarring, which surround the area of caseation in most cases of tuberculous disease. Some mild bleeding seems to come from diapedesis through the capillary walls, or from rupture of a small branch of the pulmonary artery in an area of acute exudative tuberculosis.

The second type of tuberculous hemorrhage may be profuse and, in some instances, exsanguinating. It was demonstrated by Charr and Sevacool[2] in 1940 that severe hemorrhages usually arise as a result of the rupture of a Rassmussen type of aneurism in the medial wall of a tuberculous cavity, rather than of one of the fibrotic vessels which is frequently seen crossing old tuberculous cavities. Such hemorrhages most frequently occur from the first branch of the pulmonary artery because it is anatomically related to the apex, the site of tuberculous cavitation in the adult. A cavity which extends down to the level of the second rib, near the border of the sternum should be viewed with particular suspicion, and collapse therapy should be considered as a prophylactic measure. The endoscopist can be of assistance in definitely locating the bleeding lobe, especially in cases of multicavitary disease, in order that collapse therapy may be applied to the proper parts of the lung.[3]

The third type of hemoptysis in the tuberculous individual is that from a calcified hilar node which ulcerates into the lumen of the bronchus as a result of pressure necrosis. Here we find purulent discharge associated with hemoptysis and sometimes a large amount of caseous material. This has been well described by Maier.[4] Bronchoscopically the picture is that of a single segment or bronchus from which is coming bloody and purulent material. In rare instances a broncholith may be located.[4] In these cases, the aspiration of accumulated material is advisable and may be of considerable therapeutic importance. It is well known that an accident of this sort may result in endobronchial spread of tuberculosis if the contents of the node are not entirely free from acid-fast organisms. The bronchoscopic aspiration of such material may materially reduce the danger of spread.

Bronchiectasis secondary to tuberculosis is another cause of hemoptysis which will be considered under the general heading of bronchiectasis. It differs from other forms of bronchiectasis only in its frequent location in the upper lobe.

Bronchiectasis is a disease of two distinct pathological types. Bronchiectasis sicca is a disease in which tubular, or sometimes saccular dilatation of the bronchi and bronchioles exist in the absence of purulent infection. Hemoptysis is often the first and only symptom in such cases. In this form of bronchiectasis the bleeding is usually not severe and presumably arises from small divisions of the bronchial arteries which have become hyperemic in one of the bronchiectatic areas. It is here that the endoscopist can be of considerable diagnostic help. Often the bronchoscopic picture is not unlike that

of the normal tracheobronchial tree, except that the bleeding lobe may be identified accurately in most instances if bronchoscopy is performed at the proper time in the course of the disease. In the event that the endoscopist is unable to locate the exact site of bleeding, bronchography usually will demonstrate definite evidence of bronchial abnormality thus pointing the way to further therapy.[5-7]

The suppurative form of bronchiectasis generally presents a classical history. Morning expectoration is profuse and regular, amounting in advanced cases to "bronchial vomit." The patient frequently expectorates bloody foul sputum. Bleeding in these cases is thought to arise from granulation tissue lining the dilated bronchi but may come from small divisions of the pulmonary artery. This is usually, but not always, a disease of the lower lobes, being most common in the lower lobes, next in the right middle lobe, third in the lingula, and least in the upper lobes. This is apparently the result of a simple gravitational effect which concentrates secretions in the dependent part of the lung. In most instances these infections are related to infections of the nose, adenoid, tonsils, and sinuses. There is debate as to whether discharge from the sinuses dripping down the trachea settles in the dependent portion of the lung producing bronchiectasis, or whether infection in the lung, being constantly coughed into the upper airways, produces the sinusitis. Evidence is predominantly in favor of the latter view. The accumulation of secretions in anatomically dilated bronchi which have become divested of their normal cilia, and therefore are left unprotected with inadequate ciliary activity, fosters infection. In this situation granulation tissue, slough of fragments of the bronchial cartilages, and bleeding may well and frequently does develop.[5-7]

The endoscopist has an important role in the treatment of this disease. He is able to visualize the area from which bleeding and purulent discharge are arising. In many instances he can make a diagnosis of bronchiectasis, confined to one or more lobes of one or more lungs. In the event of mechanical obstruction by secretion, bronchoscopy is of therapeutic value in relieving the obstruction. Cleansing of the tracheo-bronchial tree, followed by proper postural drainage is of considerable help in therapeusis. The necessity for cultural studies and cellular material for Papanicolaou studies to rule out malignancy, must not be overlooked, even in the apparently frank case of purulent bronchiectasis. Thus, bronchoscopy has both a diagnostic and a therapeutic value. In addition, those patients who come to surgery are greatly benefited by preoperative and postoperative bronchial aspiration as a routine part of surgical care. It is im-

perative in rare instances that these procedures be performed frequently and thoroughly.

The bronchogram is a valuable diagnostic procedure best accomplished by the cooperation of the endoscopist and the radiologist. The bronchoscopist should apply topical anesthesia to the tracheobronchial tree. Following this a catheter should be introduced into the trachea. While the patient is lying under the fluoroscope radiopaque material may then be introduced into any selected bronchus and the filling of each individual lobe carefully studied under direct fluoroscopy. Rapid spot films are of great help in these studies. Pre- and post-examination AP, lateral, and oblique films are essential. The use of iodized oil for this purpose has been standard practice for several years but is now becoming less popular and will almost certainly give way, in the near future, to some of the more rapidly absorbable water-soluble agents which do not becloud subsequent x-ray films over the course of months or years.[9, 10, 11] This technique has been well worked out by Fischer,[9] Homma,[10] and others who have obtained very satisfactory studies by using a cellulose base and by taking frequent spot films at the time of examination. The chest is frequently clear in four hours after this type of contrast medium is used. Some favorable results have been obtained by the inhalation of nebulized iodized oils which adhere to the bronchi and produce adequate bronchograms.

Pulmonary abscess is associated with hemoptosis in 49.2% of cases according to Ray.[12] This disease is usually secondary to the delayed resolution of some suppurative condition of the lung, or to the aspiration of a foreign body. It is difficult to explain the origin of such disease without pre-supposing the presence of an obstructive lesion of one of the bronchi. Bleeding is most likely to come from a small branch of the pulmonary artery but it may be profuse. It may arise either from granulation tissue lining the abscess cavity or from a pulmonary artery and may, in a significant number of instances result fatally.[12, 13, 14]

HEMORRHAGE IN PUTRID LUNG ABSCESS—E. S. RAY[12]

	57 ABSCESS CASES	7 CASES OF HEMOPTYSES DEATHS
Small Hemorrhage	11	2
Moderate Hemorrhage	9	3
Large Hemorrhage	5	2

The role of endoscopy is of unusual importance in this instance as the bronchoscopic picture of lung abscess is typical. In the first place the discharge of fetid pus is usually from a single lobe orifice, and bleeding, if present, is from the same region. The mucous membrane about the involved bronchial orifice is fiery-red but the remainder of the bronchial membrane is relatively normal. If the abscess is secondary to a foreign body, the offending object may be visualized and removed, relieving the obstruction to the bronchus, permitting the egress of pus, and frequently resulting in cure of the lesion. In some instances the diagnosis of lung abscess may be made with the bronchoscope, as in a recent case seen by the author. The dense pulmonary shadow was thought to represent a neoplasm until bronchoscopic aspiration of that region produced large quantities of pus from a fiery-red upper lobe orifice and a fluid level was subsequently demonstrated in the postoperative chest plate, making the diagnosis of cavitary pulmonary disease. The most important stage in the prevention of lung abscess is when the disease is still an unresolved pneumonia and when, by aspiration of the lobe, cavitary pulmonary suppuration may be prevented.

Abscess may occur peripheral to an obstruction caused by a carcinoma.[8, 15] Carcinoma of the bronchus is the etiologic factor in the production of hemoptysis in 53.6% cases (Abbott and Hopkins,[16] Moersch,[17] Jackson and Diamond[18]). This disease arises in the bronchial mucous membrane and for that reason its bleeding customarily originates from the bronchial arteries. It is often mild, but sometimes severe, and is the one type of bleeding which occurs repeatedly day after day for many days, weeks, or months. Most hemoptyses from other types of disease are sporadic, but once the bronchogenic carcinoma has broken down and ulcerated and the patient has begun to bleed from it, it commonly continues to bleed a little every day for long periods of time. The bronchoscopist here has an excellent opportunity to visualize the lesion and often to perform biopsy. If it is not located centrally, to permit direct visualization, it may be seen by the use of Broyles' telescopes, or may be demonstrated by microscopic study of exfoliated cells by the Papanicolaou technique (Clerf[19]). With the bronchoscope held at the orifice of the lobular bronchus a cough on the part of the patient will sometimes force a drop of blood into view, so that the region of the disease may be accurately located. In the absence of direct biopsy, gelfoam sponge biopsy or the study of aspirated secretion with the Papanicolaou or cell block techniques may provide the answer.

Metastatic Carcinoma produces bleeding in 24% of the cases.[16] Metastatic lesions are seen in the lung ten times as commonly as is

primary pulmonary carcinoma. They are spread from such tumors as renal cell carcinoma, chorionepithelioma, or carcinomata of the breast, thyroid,[20] stomach, prostate, pancreas, or uterus. Although metastatic sarcomas are less common than carcinomas, the former is the type of malignancy which is most likely to metastasize to the lung. Metastases from sarcomas usually result from blood borne cells which are filtered out in the capillary circulation of the lung. For this reason they are peripherally located in the pulmonary parenchyma. When they have progressed to the point of producing bleeding it is usually a slight streaking at first, which results from obstruction of small branches of the pulmonary artery. Somewhat more profuse bleeding results from pressure necrosis and ulceration into a bronchus with combined pulmonary artery and bronchial artery bleeding. Metastatic pulmonary lesions have not been demonstrated to produce secondary vasodilatation of bronchial vessels such as is seen in bronchial lesions. The bleeding is usually of pulmonary artery origin. Bronchoscopically the bleeding may be located in, and is usually confined to one bronchial orifice, although it may be seen arising in more than one segment of lung as such metastatic lesions are often multiple. It is in this instance that the Broyles' telescopes and the careful study of material taken for Papanicolaou examination, gelfoam sponge biopsy, and cell block studies are invaluable.

Mediastinal neoplasms are not infrequent and cause about 50% of hemoptyses.[9] These lesions are usually located in the lymphoid deposits of the mediastinum and produce pulmonary bleeding by pressure upon the hilar bronchi, with necrosis and ulceration of the membranes lining these structures. Bronchoscopically one may locate the region of the lung which is involved and may actually see other signs of the neoplasms. The carina may be thickened and widened, the angle between the right and left main bronchi may be increased and signs of bronchial compression from external pressure may be noted. Inflammatory changes in the bronchial mucosa surrounding the ulceration are suggestive of such extrabronchial disease and are relatively easy to discern. In most instances, hemoptysis comes well after there are many other signs of mediastinal disease.[21]

Chronic Bronchitis is a frequently etiologic factor in the production of hemoptysis. In this disease friable, hyperemic mucous membrane is torn by continuous coughing with resultant production of blood in 44% of cases (Abbott and Hopkins[6]). This is usually slight bleeding and arises from the smaller divisions of the bronchial arteries. In this form of bronchial disease bronchoscopic examination is of the greatest help in localizing the site of bleeding. Here

one sees a reddened, friable mucous membrane which bleeds at the slightest touch of the bronchoscope often from several widely separated areas. While bleeding arising in a solitary pulmonary lobe should make one suspicious of bronchiectasis, carcinoma, or lung abscess, generalized hyperemia and friability of the mucous membrane, in the absence of definitely localized bleeding areas, points to chronic bronchitis.[22, 23]

Thoracic trauma actually covers such diverse types of lesions that any discussion of the field in a general manner must leave something to be desired. Penetration of the lung by a fractured rib fragment is not necessary to cause hemoptysis, but blast, or a crushing injury, in the absence of rib fracture, may still produce ecchymosis and hemorrhage of the pulmonary tissue. Bleeding from this sort of lesion is apt to be diffuse or to ooze from small branches of the pulmonary artery and bronchoscopically may be seen as coming from more than one bronchial orifice and often from more than one lung. In some instances, bronchoscopy may save the lives of these patients by preventing the accumulation of blood and other secretions from obstructing the bronchi. This is especially true in the case of a fixed chest, when the patient is reluctant or unable to cough because of pain.

Injuries of the chest resulting from penetration of fractured ribs, gunshot, and stabbing, produce a different type of pulmonary bleeding, in many instances. Many of these are relatively circumscribed injuries. They do not as a rule produce generalized lesions. In most instances they damage both the bronchi and the parenchymal pulmonary tissue, thus producing bleeding from both bronchial and pulmonary arteries in varying amounts. These patients usually have relatively normal appearing bronchial membranes, but often show evidence of tracheal or bronchial displacement due to the accumulation of air or fluid in the pleural spaces. The aspiration of blood and abnormally copious secretions from the airways may be beneficial in the therapy in these cases. The identification of the injured area of pulmonary tissue can, in most instances, be made more efficiently in some manner other than by bronchoscopy.

It must not be forgotten that frequently the blast type of pulmonary injury is seen associated with the penetrating type of lesion, so that a pure type is not always seen in these cases.

Empyema like bronchiectasis, is one of the pulmonary suppurations which results from the incomplete resolution of pneumonia or the contamination of a pleural effusion and its subsequent incomplete healing. It is essentially an intrapleural abscess which mechan-

ically presses upon the area of adjacent pulmonary tissue and prevents its proper expansion. It is the result of this pressure that produces most of the hemoptysis seen in this disease (24.5%). Bleeding is commonly scanty in the early phase and arises from the pulmonary artery due to interference with normal venous flow. However, as the disease progresses and involvement of the bronchus occurs, ulceration of the bronchial membrane may take place and bleeding from the bronchial vessels may begin before, simultaneous to, or following the development of a bronchio-pleural fistula. The bronchoscopic picture is that of a lung abscess, with the production of blood-streaked purulent discharge from a single fiery-red bronchial orifice. However, there is occasionally more than one bronchial orifice involved, rather than the single orifice usually found in the lung abscess.

Cardiac lesions are less frequently the cause of hemoptysis. There are three types of hemoptysis seen in association with cardiac disease.

The non-decompensated heart produces hemoptysis rather rarely. This bleeding is not anticipated as a rule. However, mitral stenosis, in the absence of a history and of physical signs of decompensation, or pulmonary infarction, accounts for the bleeding in 10% of all adults. It occurs chiefly in young or middle-aged rheumatic individuals who frequently are unaware of their rheumatic history. The bleeding usually is secondary to severe physical or emotional strain and is characterized by the production of a large quantity of blood at one time, followed by blood streaking for several days. It is thought that a sudden increase in intrathoracic pressure added to a high pulmonary blood pressure, especially in the presence of pulmonary artery arteriosclerosis, is the etiology of the bleeding. Tortuous varices of the bronchial veins in the submucosa of the bronchi, the bronchopulmonary anastomoses, have been demonstrated in rheumatic humans with mitral stenosis.[24] The prognosis in these cases is usually good but recurrences are quite common.[25, 26]

Bronchoscopically the bleeding is profuse, usually coming from a relatively large rent in the broncho-pulmonary vessels, often confined to one bronchial lobe. Aspiration and prevention of atalectasis is all that can be accomplished by bronchoscopy in these cases.

Acute heart failure, especially left-sided heart failure, produces quantities of frothy sputum, which is usually blood-tinged. In this case the blood is accumulated in the edema fluid by diapedesis of red cells through an over-distended pulmonary venous circulation and, for this reason, the entire pulmonary tree is equally involved. Bronchoscopy is not commonly used to alleviate the accumulation of edema fluid, but in rare instances it, or tracheal suction, must be

utilized. Endoscopy is useful merely to remove the massive obstruction. The picture is that of bloody froth pouring from every bronchial orifice. If such a procedure can limit the hypoxia until compensation can be accomplished by means of the cardiac drugs, it is possible that no further difficulty will be encountered. This bleeding is from capillaries and is of pulmonary vein origin.[27]

Emboli arising in the heart or in the peripheral venous circulation and passing through the heart into the lung with subsequent infarction, produce another group of hemoptyses of circulatory origin. In 44% of pulmonary infarcts, there is hemoptysis. When an embolus obstructs the pulmonary artery, or one of its divisions it produces a wedge-shaped area of necrosis peripheral to it, with the apex of the wedge located centrally and the base peripherally. Bleeding in this instance is usually streaking of the sputum and small amounts of old, dark blood, rarely profuse hemorrhage. The bronchoscopic picture in these cases is that of bleeding areas confined to one lobe or to one region. There may be multiple emboli, and multiple areas of hemorrhage in different lobes.

Bronchial adenoma, with bleeding in 100% of cases, is one of the more commonly considered lesions, although of relatively uncommon occurrence.* It is a development within the bronchial mucous membrane of an adenoma consisting largely of bronchial glands and blood vessels. Its status, as to malignancy, is debatable, but its role in producing bleeding is established. Because it arises in the bronchial mucous membrane, the bleeding comes from the bronchial arteries. Hemorrhage is usually sporadic and is not, as a rule, profuse, although exsanguinating hemorrhages have been reported. By means of the bronchoscope and the telescope blood is seen coming from a single bronchial or segmental orifice and frequently one is able to obtain tissue for biopsy from a directly visualized tumor.[28, 30]

Pneumonia is one of the diseases responsible for the production of hemoptysis and, in years gone by, was one of the most common sources of bloody sputum. Today there appears to be a marked decrease in the occurrence of lobar pneumonia but those cases which do occur still seem to produce the typical "rusty" or "prune juice" sputum. Pneumonia patients with abnormal hemoptysis, i.e., those

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Since preparation of this article a report has appeared, of a series of 100 cases of bronchial adenoma of which 17 were asymptomatic.[34] Thus the 100% occurrence of hemoptysis described in this paper is far too high. In many instances hemoptysis is the first sign of bronchial adenoma but it is obvious that many early asymptomatic masses are being noted today and it is possible for obstructive signs to occur before hemoptysis. Thus hemoptysis is an important sign of bronchial adenoma, but is not necessary to the diagnosis.

lasting more than 24 hours, or not remaining classical as to "prune juice" quality, should be investigated bronchoscopically, and otherwise, to determine the source of the bleeding. It is still a disease to be reckoned with, and one which may need the aid of the endoscopist. The bronchoscopic picture of the disease is that of one or more bronchial orifices, reddened and full of rusty, purulent discharge. The blood probably arises from diapedesis of red cells from both the bronchial and the pulmonary vessels. Bronchoscopy, in this instance, is more likely to be needed to aid in the resolution of the pneumonic process, than to identify the source of the bleeding. Judicious bronchoscopy may well prevent the development of lung abscess, bronchiectasis, or empyema which often result from faulty resolution of pulmonary suppuration and inadequate expansion and aeration of alveolar tissue.

Pneumonitis is a cause of hemoptysis in 50% of nonspecific cases. These fall into the group of smaller hemorrhages. Bleeding in these cases is usually streaking of the sputum and comes about by bleeding of the small bronchial and pulmonary vessels which have become hyperemic and unusually friable in the course of an inflammatory disease. Viral pneumonitis, lipoid pneumonitis, and bacterial pneumonitis all run a similar course. Bronchoscopy reveals blood streaked discharge coming from the lobe or lobes involved and is sometimes of considerable help diagnostically, by collecting material for microscopic and bacteriological study. In addition, the therapeutic lift, which aspiration produces, is sometimes of considerable importance.

Idiopathic hemoptysis is one relatively common form of hemoptysis reported by almost every author dealing with this subject. Numerous series have been studied to determine the etiology. In many instances hemorrhages have occurred in apparently healthy individuals who have had no history of antecedent pulmonary disease. The bleeding may have been an isolated instance or may have been repeated, and yet no etiologic factor can be determined. Theoretically it may arise from either the bronchial or pulmonary vessels and may occur in any part of the lung. The bronchoscopic picture is that of a completely normal tracheobronchial tree, with, or without, the presence of blood. In those in which blood is demonstrated, it is usually confined to one lobular orifice and is merely seen coming from it. Even in the absence of a demonstrable cause these patients usually get along well, without subsequent difficulty. In only a very small percentage of cases do pathological lesions later make themselves manifest.[31, 32, 33]

	Chaves	Moersch	Jackson	Cameron	Saunders
Patients	325	200	436	70	105
Idiopathic Hemoptysis	189	17	34	8	19
Per Cent	58.1	7.5	7.8		18.0
Chronic Bronchitis		18	74		
Per Cent		9.0	16.9		

It is of interest to speculate concerning the nature of these lesions. Such a lesion would be a small localized area of bronchiectasis, a small bronchial ulceration beyond the vision of the bronchoscope, a tiny hemangioma, or an arteriovenous aneurism.

Numerous unusual causes of hemoptysis have been reported in the literature. While they deserve mention they do not enter into the serious consideration of bronchoscopic problems because of their relative infrequency. The bleeding may be from either bronchial or pulmonary vessels, and in some instances may arise from both.

The following list of unusual causes is reported merely for completeness:

Foreign body
Asthma
Bronchial ulcer
  Non-tuberculous
Atalectasis
Diaphragmatic hernia
Fungus infection
Sinusitis
Pulmonary fibrosis
Emphysema
Pneumatocele
Silicosis
Bronchial endometriosis
Broncholith
Lipoid pneumonitis
Hematoma of lung
Endobronchial polyp
Shrapnel in heart
Fat embolism
Trichinosis
Caisson disease—air sickness
Neurofibroma of thoracic wall
Thyroiditis
Hypertension
Suture in bronchial stump
Pulmonary sarcoidosis
Loeffler's syndrome
Nonspecific bronchial granuloma
Streptothricosis
Chondroma of bronchus
Osteoma of trachea
Dermoid cyst communicating with trachea
Blood Dyscrasia
  1. Leukemia
  2. Polycythemia
  3. Pernicious Anemia
  4. Capillary fragility—avitaminoses
Exploratory needling
Bubonic plague
Bronchial fluke
Hydatid cyst
Amebic abscess of liver with
  bronchopleural fistula
Fibroma of lung
Chronic granuloma of lung
Hereditary telangiectasis
Avitaminosis—Tersild—Vit P

The source of bleeding has been statistically related to the anatomical studies by Abbott.[10] His compilation follows:

Right upper lobe	63	Frank hemoptysis	318
Right middle lobe	30	Scanty	174
Right lower lobe	75	Exsanguinating	
		Degree undetermined	5
Total right lung	217	Total	497
Left upper lobe	82		
Left middle lobe lingula	20	Male patients	745
Left lower lobe	92	Hemoptysis in males	286
		Female patients	562
Total left lung	212	Hemoptysis in females	211
Bilateral	74	Total chest patients	1316

This gives considerable insight into the anatomical location of pathological changes. Most common is lower lobe, of bronchiectatic origin, and, next is upper lobe, of tuberculous origin.

SUMMARY OF TYPES OF HEMOPTYSIS

DISEASE	BLEEDING—Type				ANATOMICAL SOURCE		
	Recurrent	Episodic	Streaking	Profuse	Bronchial Artery	Pulmonary Artery	Pulmonary Vein
Tuberculosis	X	X	X	X	X	X	
Bronchiectasis sicca		X	X		X		
Bronchiectasis suppurative	X		X		X		
Pulmonary abscess		X	X	XXX	X	XX	
Carcinoma	XXXXX		X		X		
Chronic bronchitis		X	X		X		
Mediastinal neoplasms		X	X	X		X	X
Trauma	X	X	X	X	X	X	X
Empyema	X		X			X	X
Cardiac		X			X	X	X
Adenoma		X	X	X	X		
Pneumonia	X		X		X		
Pneumonitis		X	X			X	X
Idiopathic	X	X	X	X	X	X	X

SUMMARY

Hemoptysis is a cardinal sign of potentially serious disease, which cannot be ignored. It is essential to differentiate pulmonary from other sources of hemorrhage. The amount of blood expectorated is no index of the gravity of the underlying pathology. In this investigation, endoscopy has an important role and must be utilized in its proper sequence. Following careful history, physical examination, x-ray examination, and laboratory studies of the sputum, bronchoscopy should be performed and orifices of all bronchi should be examined. Secretion should be aspirated and biopsies done where possible. Bronchial aspirates should be examined microscopically and bacteriologically, and the findings correlated with the remainder of the pathological findings, determined by other means. Bronchography and spot film techniques should be utilized to visualize the small divisions of the bronchial tree employing one of the water-soluble contrast media.

Although hemoptysis is usually associated with some demonstrable lesion, there are a number of cases which reveal no pulmonary pathology and in which no disease develops subsequently. This group of cases is significantly smaller in series which have been more meticulously studied and for that reason, exhaustive studies should be made before accepting the diagnosis of idiopathic hemoptysis.

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XXVIII

CHLORAMPHENICOL-BORIC ACID POWDER IN THE TREATMENT OF OTITIC INFECTIONS

A CLINICAL REPORT

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The advent of sulfonamides and the antibiotics greatly advanced the treatment of most otitic infections, yet they continue to be a disturbing problem in the everyday practice of otorhinolaryngology. It[1] has been estimated that infections of the external auditory canal alone constitute from 5 to 40 per cent of all cases of ear disease seen in otologic practice in the United States, the wide differences in percentages being due to sectional variations. A discharging ear may be a social handicap and frequently impairs hearing. To quote Sullivan and Smith,[2] "A chronic discharging ear which can be made dry with office treatment is indeed gratifying to the patient." Parenthetically, it also gratifies the physician. Many new drugs have been offered for the treatment of these diseases. Some have proved beneficial. The purpose of this report is to present clinical experiences with chloramphenicol and boric acid in the treatment of otitic infections. Bacteriological studies will be presented which help to explain the beneficial results noted in patients treated with this mixture of powders.

In past years, there has been emphasis on various fungi as the etiological agents in otitis externa[3-11] but this concept has changed. Many articles have appeared in the literature to support this statement.

Hayes and Hall[12] reported that the resistant etiological bacterium in chronic suppurative otitis media and external otitis was predominantly Pseudomonas aeruginosa (Bacillus pyocyaneus) in one hundred cases studied.

According to Fowler,[13] cultures taken from the ear canals of patients who have chronic otitis media or discharging cavities fol-

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Presented as candidate's thesis to the American Laryngological, Rhinological and Otological Society.

lowing radical mastoidectomy contained many of the same type of organisms found in external otitis by Senturia[14] and others.[15, 16]

Staphylococcus was the predominating organism in clutures of otitis externa in reports by Gill,[1] Friedman and Hinkel,[15] Douglas[17] and Alonso.[18]

In a study on the use of strepotmycin in the treatment of diffuse external otitis, Senturia and Broh-Kahn[19] reported that all infected ears (53 patients—106 ears) showed gram-negative rods as the predominant organisms; by far the largest percentage of ears showed cultures of Pseudomonas oraganisms. Occasional strains of Alkaligenes, Aerobacter and Proteus were identified. The high incidence of gram-negative bacilli in cultures obtained in otitis externa has been stressed in other reports.[14, 20-35]

The importance of streptococci as pathogenic agents in otitis externa was observed by Michell,[36] Ponce de Leon,[37] and Williams, Montgomery and Powell.[38]

According to Senear,[39] the fungi demonstrable in the ear are usually of non-pathogenic varieties and rarely of types giving rise to the usual dermatologic disorders of mycotic origin.

It can be concluded from these reports that the etiological agent of otitic infections is most frequently a bacterial infection of either gram-positive or gram-negative organisms or a mixed infection of both gram-negative and gram-negative organisms.

In the treatment of otitic infections many clinicians have reported the use of an agent, such as chloramphenicol, which is effective against both gram-positive and gram-negative bacteria.

Welsh and Lewis[40] stated that the therapeutic value of chloramphenicol, indicated by laboratory studies of the activity of this drug, has been in large part borne out by clinical trial. Chloramphenicol, a wide-spectrum antibiotic, is active against both gram-positive and gram-negative bacteria, certain rickettsia, spirochetes, and viruses. Fungi and protozoa are not affected by its use.

Raper[41] remarked that in mixed surgical infections chloramphenicol extends the bacterial range of penicillin but does not have the injurious effect on the cochlear and vestibular systems frequently seen with streptomycin and dihydrostreptomycin.

Romansky, et al.,[42] in a study including eleven of the most common pathogens, found more strains sensitive to chloramphenicol than to any other of the five most widely used antibiotics.

Mitchell, Arnold, and Lett[43] made determinations of the sulfamylon (p. amino-methylbenzene-sulfonamide) and antibiotic sensitivities of 54 cultures of Pseudomonas aeruginosa isolated from cases of otitis externa. Fifty-two cultures of the Pseudomonas aeruginosa studied were susceptible to sulfamylon, 45 isolations were susceptible to chloramphenicol, and 19 isolations were susceptible to oxytetracycline (Terramycin®). Dihydro-streptomycin and streptomycin showed a poor degree of activity. Penicillin, chlortetracycline (Aureomycin®), and bacitracin were not effective.

Coppleson[44] treated infected wounds and ulcers by direct application of crystalline chloramphenicol and by irrigation, with "most impressive" results. He remarked that this is a most valuable therapeutic method, and that the antibiotic is probably more efficient when applied directly to open wounds than when administered by mouth.

Magauran[45] confirmed Coppleson's observations. Chloramphenicol was used "topically in many cases of external otitis, chronic suppurative otitis media and resistant infections of fenestration and mastoid cavities with impressive results."

Alderson[46] also confirmed Coppleson's observations on the efficiency of the local application of chloramphenicol. He found a one per cent chloramphenicol solution soaked on ribbon gauze and inserted as a pack into the external auditory canal to be most beneficial in cases of external otitis.

In a later communication, Magauran[47] recommended the insufflation of the powder by puncturing each end of a chloramphenicol capsule and blowing. He[48] described two simple insufflators that he has designed for this purpose.

Lewis and Gray[49] used locally a 10 per cent solution of chloramphenicol in propylene glycol in cases of infected mastoid cavities and chronic suppurative otitis media. They used either wicks left in place for 48 hours or drops instilled two or three times a day. These authors found that a 10 per cent solution of chloramphenicol was "bactericidal to practically every organism occurring in chronic otorrhea—even where Pseudomonas pyocyanea was the infecting organism." In another report they[50] used a 15 per cent solution of Chloramphenicol in propylene glycol in a similar manner.

David[51] reported beneficial results from the topical application of chloramphenicol cream in otitis externa, chronic suppurative otitis media, and infected mastoidectomy cavities. The cream was prepared by mixing four grams of chloramphenicol with one ounce of

unibase. Unibase contains higher fatty alcohols—petroleum, glycerin, water and an emulsifying agent—in such proportions that incorporation of both water soluble and water insoluble drugs is accomplished with ease.

In a series of seventy radical mastoidectomies Jones[52] skin-grafted the cavities with Thiersch grafts and then packed the cavities with gauze soaked in 10 per cent chloramphenicol in propylene glycol. In addition, chloramphenicol 250 mg was given orally every six hours during hospitalization. The formation of a dry, well epithelialized cavity was noted as well as a reduction in the duration of stay in the hospital and the total time under treatment.

Ausband and Harrill[53] isolated 15 strains of organisms, principally staphylococci, diphtheroids, Pseudomonas aeruginosa, Proteus mirabilis, and Aerobacter aerogenes, from patients with otitis externa and otitis media. Chloramphenicol was applied locally as follows: Five drops of a solution of chloramphenicol was instilled in the affected ear four times a day. The solution was prepared by adding the contents of a 2 cc ampoule containing 0.5 gm of chloramphenicol in acetyl dimethylamine to 28 cc of 70 per cent alcohol. In 78 per cent of 49 patients with 53 infected ears who returned for follow-up study, the ears became dry, 17 per cent of the others showed marked improvement; and no change was noted in 5 per cent. Three patients showed a sensitivity reaction.

Good results in the treatment of chronic otitis media from the topical administration of chloramphenicol were reported by Heimendinger and Lafon[54] and Didier, Vouters and Klaas.[55]

The topical application of chloramphenicol has been reported to be beneficial in the treatment of eczema and pruritus of the ear canal,[56] superficial and deep pyodermas,[57] various pyogenic dermatoses[58] and a wide variety of wounds infected by penicillin-resistant or insensitive oragnisms.[59]

It has been emphasized that the normal acidity of the skin of the external auditory canal is of importance.[60, 61] The pH of the skin of the diseased external auditory canal is usually alkaline.[62-64] McLaurin[65] remarked that in cases of otitis externa there are two important factors influencing the disease, namely: interruption of the continuity of the epithelial lining and alteration of the pH from the acid to the alkaline side.

METHOD AND TECHNIQUES

Thorough cleaning and drying of the external auditory canal before applying any medicament is of prime importance. As Mc-

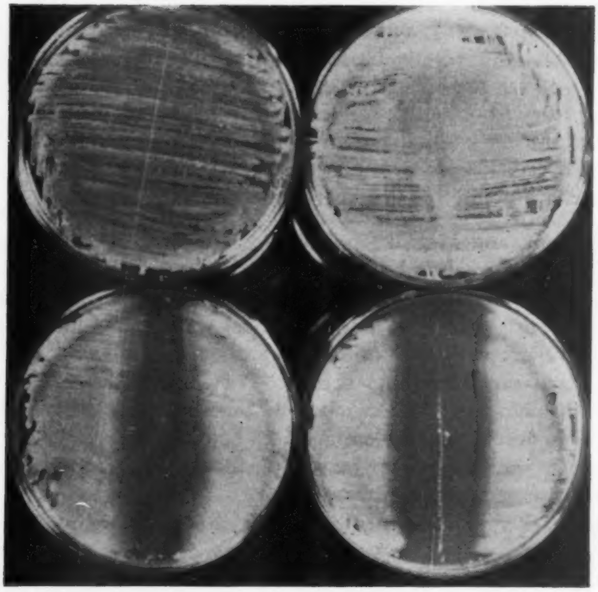

Fig. 1.—A culture was obtained from a patient with left acute otitis externa (Case No. 3, A. H. F.) and suspended in 7 cc of brain heart infusion agar. Four blood agar plates were inoculated with this suspension. Plate No. 1 was left as a control. Plate No. 2 was streaked across its center with a loopful of boric acid powder. Plate No. 3 was streaked across its center with a loopful of chloramphenicol powder. Plate No. 4 was streaked across its center with a loopful of chloramphenicol-boric acid powder mixture (1:4). The plates were incubated for 18 hours and the above photographs obtained. The streak plates contained colonies of hemolytic Staphylococcus aureus and Pseudomonas aeruginosa.

Laurin[65] stated, "Moisture, maceration and the accumulation of epithelial debris and dead tissue all offer excellent conditions for the growth of organisms and for the production of an alkaline environment favorable to their growth. The removal of debris brings to pass another requirement for effective treatment, that which ever agent is used must be brought into intimate contact with the tissues."

According to Saunders,[66] the ideal agent for the treatment of aural infections should have the following properties: 1) it should be strongly effective against gram-negative organisms; 2) it should be easy to apply and should not interfere with the elimination of discharge or debris; 3) it should be in an acid medium; 4) it should have a drying effect and 5) the vehicle used with the agent must not impair its efficiency. To this list the following should be added: 6) the agent should be strongly effective against both gram-positive and gram-negative organisms (a potent broad-spectrum antibiotic); 7) it should be free of toxic, irritating, or allergenic potentialities.

Following the reports of Wright[67] on chlortetracycline (Aureomycin) powder and Saunders[66] on dihydrostreptomycin-boric acid powder, an investigation was begun by the author on the use of chloramphenicol-boric acid powder in the treatment of otitic infections. This mixture meets all of the above-outlined requirements as an ideal therapeutic agent. The crude powder of chloramphenicol has been reported to have occasional, local irritating effects by Magauran,[68] and Ausband and Harrell.[53] Boric acid powder therefore was added to reduce this undesirable quality. Boric acid powder also has a drying effect. In this clinical study a mixture was used of four parts of boric acid U.S.P. and one part of chloramphenicol.

The pH of the substances used was found to be as follows:*

boric acid powder, U.S.P. (saturated solution)—pH 4.3
chloramphenicol powder (water slurry)—pH 6.0
chloramphenicol-boric acid powder (1:4 water slurry)—pH 4.0

This mixture of these two powders appear to aid in maintaining the desirable pH of aural epidermis.

The present clinical study consisted of 53 patients, with 78 ears effected by diffuse otitis externa as classified by Senturia,[69] 12 patients with 13 ears affected by chronic suppurative otitis media, and 4 patients with old, infected radical mastoidectomy cavities. Diffuse

*The determinations were made with the Beckman Glass Electrode pH Meter (Model G). The solutions were at a room temperature of 23° centigrade and freshly distilled water was used.

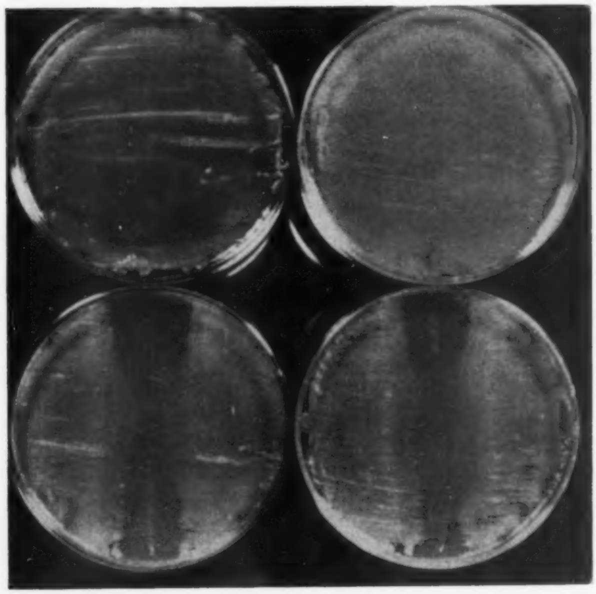

Fig. 2.—A culture was obtained from a patient with right acute otitis externa (Case No. 6, D. O.) and suspended in 7 cc of brain heart infusion agar. Four plates were inoculated with this suspension. Plate No. 1 was left as a control. Plate No. 2 was streaked across its center with a loopful of boric acid powder. Plate No. 3 was streaked across its center with a loopful of chloramphenicol powder. Plate No. 4 was streaked across its center with a loopful of chloramphenicol-boric acid powder mixture (1:4). The plates were incubated for 18 hours and the above photographs obtained. The streak plates contained colonies of Streptococcus viridians, Pseudomonas aeruginosa and Neisseria catarrhalis.

otitis externa occurred in 19 acute and 59 chronic cases. All of these patients were seen consecutively in private practice.

The following was the procedure used: The external canal was thoroughly cleansed. This was accomplished by irrigation with lukewarm 70 per cent alcohol or 38 per cent saline[70] in a 2 oz. DeVilbiss bottle, or by means of suction, or a cotton-tipped applicator soaked with 70 per cent alcohol. The external canal was then dried and chloramphenicol-boric acid powder (1:4) from a DeVilbiss powder-blower, was carefully insufflated into the canal. The entire canal wall and the drum head were "frosted" with the powder. It was unnecessary to insufflate a surplus amount of the powder. The patient was instructed to leave the ear untouched and not to allow the entrance of water. Office visits were usually every four to five days except in the severe acute cases of otitis externa, which were seen more often. In acute cases, pain was relieved by narcotics or roentgen therapy as recommended by McLaurin.[71] In cases of otitis externa complicated by furnuculosis, low-dose staphylococcus toxoid as recommended by Hansel,[72] or roentgen therapy was given. In attempting to restore the normal status of the structure of the ear canal, it was frequently necessary to restore depleted lipoids as reported by Senturia.[73] Ten per cent boric acid in anhydrous lanolin was prescribed for local application at home. In cases of old, infected radical mastoidectomy cavities and chronic suppurative otitis media, granulation tissue was curetted or cauterized with trichloracetic acid before insufflating the powder. The patient was not discharged until the ear had been free of discharge for a month.

Although routine bacteriological studies are not uniformly practical in private practice as McLaurin[74] and Senturia[70] have pointed out, if considerable improvement did not occur after the first treatment, cultures were obtained and sensitivity tests requested. Where cultures were secured, the results were in agreement with the more recent reports in the literature.

Fig. 1, Fig. 2 and Fig. 3 show the bacteriological growth in three studies of chloramphenicol-boric acid powder establishing chloramphenicol as a potent broad-spectrum antibiotic.

RESULTS

In 89 of 95 infected ears (representing 69 patients), the ears became dry. Improvement was noted in three ears. Each of these patients was considerably improved after two treatments but did not return. No change or a failure was noted in three ears. In 17 of the cases of acute otitis externa, the ears became dry and the patients offered no further complaints. In 57 of the cases of chronic

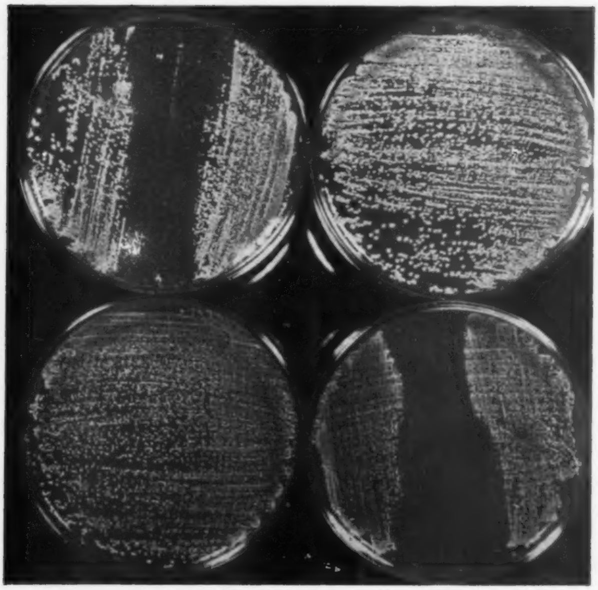

Fig. 3.—A culture was obtained from a patient with right chronic suppurative otitis media with a posterior central perforation (Case No. 54, N. J. H.) and suspended in 7 cc of brain heart infusion agar. Four blood agar plates were inoculated with this suspension. Plate No. 1 was streaked across the center with a loopful of chloramphenicol powder. Plate No. 2 was streaked across its center with a loopful of boric acid powder. Plate No. 3 was left as a control plate. Plate No. 4 was streaked across its center with chloramphenicol-boric acid powder mixture (1:4). The plates were incubated for 18 hours and the above photograph was obtained. The streak plates contained colonies of Staphylococcus aureus and Neisseria catarrhalis.

otitis externa, the ears became dry and the patients presented no further complaints. In all the patients with chronic suppurative otitis media with central perforations (12 ears), the ears became dry and clean. No improvement was noted after treatment in one case of chronic suppurative otitis media with a marginal perforation. In three of four patients with infected radical or modified radical mastoidectomy cavities, the ears became dry and clean.

TABLE I.

DIAGNOSIS AND RESULTS IN 69 PATIENTS, WITH 95 INFECTED EARS TREATED WITH CHLORAMPHENICOL-BORIC ACID POWDER.

	NO. OF PATIENTS	NO. OF EARS	DRY	APPROX. PER CENT	IMPROVED	APPROX. PER CENT	NO CHANGE	APPROX. PER CENT
Diffuse Otitis Externa								
acute	16	19	17	89	2	11		
chronic	37	59	57	96	1	2	1	2
Chronic Suppurative Otitis Media								
central perforation	11	12	12	100				
marginal perforation	1	1					1	100
Infected radical or modified radical mastoidectomy cavities	4	4	3	75			1	25
Totals	69	95	89	94	3	3	3	3

SUMMARY

This clinical study supports previous reports to the effect that otitis externa is a bacterial disease. It confirms previous observations on the beneficial results from the topical application of chloramphenicol in otitic infections. A wide-spectrum antibiotic is indicated in their treatment because of the variety of causative organisms. In using this powder mixture basic principles of treatment were followed. Careful cleansing and proper hygiene of the external auditory canal

are still very important. It is essential to relieve pain in cases of acute otitis externa. The maintenance of dryness and a normal acid pH of the external auditory canal play an important part in preventing recurrence.

Chloramphenicol-boric acid powder (1:4) is stable, acts on bacteria independently of their gram characteristics (broad-spectrum antibiotic), and is free from irritating effects on normal and infected skin and mucous membranes. No clumping or caking was noted with this mixture as with chlortetracycline (Aureomycin) and oxytetracycline (Terramycin). No signs of new infections due to nonsusceptible organisms such as candida (monilia) were noted. Chloramphenicol-boric acid powder mixture (1:4) was successful in the therapy of a majority of cases with otitic infections.

CONCLUSIONS

Chloramphenicol-boric acid powder mixture (1:4): 1) Has a desirable acidity (pH 4.0); 2) Is a potent broad-spectrum antibiotic; 3) Is free from undesirable side effects; 4) Is a useful addition to therapy of otitic infections.

My appreciation is expressed to Roland Z. Farkas, Ph.D., Tech. Director, Texize Chem. Inc., for his help with the pH determinations; Miss Jane Earle and Mr. R. G. Harris, Medical Technologists, Department of Bacteriology, Greenville General Hospital for their help in the vitro studies in this clinical study; Mrs. Jeroline Rice, Photographer, Greenville General Hospital for the photographs, and Dr. J. P. Gray and Mr. F. E. Willson of Parke-Davis & Co. for their cooperation.

Translations of papers appearing in foreign journals were made by the Literary Research Departments of the American College of Surgeons and the New York Academy of Medicine.

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The Scientific Papers of the American Laryngological Association

XXIX

THE USE OF STAPHYLOCOCCUS TOXOID IN OTOLARYNGOLOGY

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The following clinical observations on the use of Staphylococcus toxoid in otolaryngology are presented as a preliminary report, as further investigation must be conducted with the correlation of bacteriologic, immunologic, cytologic and hematologic studies.

For many years we[1] have emphasized the value of cytologic studies of the secretion of the respiratory tract in the diagnosis of allergy and of infection. More recently, Bryan[2] has shown that changes in epithelial cells of the respiratory secretions may be considered as characteristic of virus infection. With the introduction of the antibiotics, there has been a change in the patterns of infection as well as some alteration of virulence of certain organisms. The use of routine bacteriologic studies in the practice of otolaryngology is imperative today, and the development of effective vaccine therapy is now just as important if not more so than previously.

During the past 50 years various antigenic and allergenic agents such as bacterial, fungus and virus vaccines, non-specific proteins, chemical agents, pollens, dusts, etc.—have been introduced into the field of therapy, chiefly as injectable substances. The therapeutic application of these various agents has been based upon the principle of developing the tolerance of the patient by beginning with a small dosage and increasing it gradually until satisfactory results were obtained. If an exacerbation of symptoms or a focal reaction occurred, either the dosage was reduced or the treatment was discontinued. In other instances general reactions were noted to appear usually only after the larger doses had been given. With certain agents employed in the treatment of specific conditions, good results have been obtained. On the other hand, many failures have been encountered, and yet in general there has been no tendency to modify the original principle of this "build-up" type of dosage.

The principle of the use of the small optimum effective dose, especially in the injection of vaccines was introduced as long as forty years ago but the method never received general recognition in spite of the fact that it offered many advantages such as the absence or avoidance of all types of reactions, as well as a high percentage of good therapeutic results.

In certain infectious diseases, such as measles, mumps, scarlet fever, small pox, typhoid fever, poliomyelitis, etc.—long lasting or permanent immunity either follow the attack or may be induced artificially in some instances by the injection of vaccines. By the use of vaccines, some of these diseases may be reproduced but the ideal method is one by which it is induced in a very attenuated rather than in the severe natural form. There are many infectious conditions such as those which affect the respiratory, intestinal, genitourinary tract, the skin and special organs, caused by a variety of gram-negative and gram-positive organisms for which vaccine therapy has proved to be either non-effective or if so, of very short duration. For these conditions the antibiotics have been most effective.

Although the very great therapeutic value of the antibiotics is appreciated there is evidence that their use is being abused in that they are administered in instances in which they are not indicated or are given in too large doses, sometimes over a long period of time. Allergic and other side reactions especially those resulting from the disturbance of the normal flora of organisms in the respiratory and gastrointestinal tracts and the development of antibiotic resistant strains, are not infrequently encountered.[3] Secondary monilial infections involving, particularly, the mouth and gastrointestinal tract may also complicate the picture.

With the wide-spread use of the antibiotics, there has appeared clinical evidence of a decrease in immunity or resistance to infection, especially in the respiratory tract. We have encountered a significant number of instances of repeated upper respiratory infections and pansinusitis in young children, especially in those to whom antibiotics, and particularly nose drops, have been administered repeatedly. Some of these children have not passed through the normal course of a cold or sore throat without antibiotics. Since the acute infection has been attenuated in this manner, there is no definite stage of resolution reaction, at which time the acute process quickly improves and subsides. The natural immunity to the organisms concerned is

not stimulated or increased so susceptibility to reinfection occurs. In many cases in which reinfection occurred, especially during the fall and winter, we noted a high incidence of residual sinusitis. Large quantities of muco-pus could be evacuated by suction or by displacement and suction. It is evident that these children never recovered completely from the head colds, so the residual infection in the sinuses also played a part in reinfection.

In the adult we have encountered a significant number of cases of monilial infections of the mouth, tongue, tonsils, soft palate and pharynx, secondary to the use of antibiotics. In several instances a recurrence of this infection reappeared if antibiotics were taken as long as six to twelve months later. In two cases, the ingestion of beer after many months, reproduced a marked glossitis and stomatitis. From these observations it is apparent that the restoration of the normal flora of bacteria may be a slowly delayed process.

Although there has always existed a great need for effective methods of immunization to the common bacterial infections, such as colds, sore throats, pneumonia and various types of skin infections especially those caused by the staphylococcus, with the introduction of the antibiotics that need has become much greater. In a large percentage of the cases of infection of these types, because of their mildness, the use of antibiotics is not indicated. On the other hand an effective vaccine would be not only indicated but also preferred. Its use may be imperative in those instances in which the antibiotics are not tolerated. A type of therapy in which smaller doses of antibiotics may be administered to attenuate the infection combined with the use of effective vaccine dosage offers the possibility of a more safe and sane method of treatment, which is not likely to be followed by the above complications.

In discussing the matter of chemotherapy, Mellon[4] emphasizes the importance of not neglecting the stimulation of the natural defensive powers. His presentation on the relation of so-called "host factors" in modern chemotherapy are worthy of consideration. In 1935, Mellon[5] reported his observations on the use of antistreptococcal serum for the purpose of depriving hemolytic streptococci of their virulence. Of a series of 125 patients with severe subacute infections from this organism which usually caused a fatal outcome in many instances, 90 per cent recovered with the use of this serum.

It was believed that the effects obtained were not the result of specific antibodies contained in the serum, because the doses which produced maximum effects were very small, averaging from 0.01 cc to 0.10 or 0.20 cc. The majority of the patients in this series exhibited varying degrees of sensitivity to horse serum. It was noted incidentally, that a mild degree of serum sickness often heralded the early and complete recovery of the patient. This was especially true when this complication disguised itself as an arthritis. The action of specific antibody also could not explain Mellon's observation of the healing of varicose ulcers of long-standing which had become infected with the erysipeloid type of hemolytic Streptococcus. Neither could the clinical responses manifested by a leucocyte rise as well as an increase in blood calcium, blood phosphate and sometimes the chlorides, be attributed to an antiserum. There was also a disappearance of general and local edema associated with severe infections. Mellon believes that the mechanism of action is a "desensitizing" or an "anti-shock" effect. He refers to the good results previously reported from the production of hyperpyrexia and the use of nonspecific protein, especially when these agents were not employed in too large doses. The production of shock reactions from overdosage were responsible for obscuring the undoubted clinical value associated with the small, desensitizing doses, which presumably are anti-shock in effect. The size of the dose therefore, must be considerably under the toxic or shock threshold. Mellon also found that the nonspecific effect could be produced by antidiphtheritic serum as well as antistreptococcic serum. Apparently, antibodies, tissue enzymes or other antibacterial substances are liberated when the small optimum dose is employed. The reaction may be nonspecific and the response of the "anamnestic" type.

Ehrich[6] has demonstrated experimentally that large doses of antigen depress the immune mechanism and localize the antigen with damaging tissue effects. Antibody response is depressed, as manifested by the prevalence of large monocytes and histocytes. Low doses result in antibody production as shown by the predominance of lymphocytes and plasma cells.

Although various bacterial and virus vaccine preparations have long been in use, there has been in general a lack of a standardization of materials as well as dosage. Since there is always some variation in individual responses or a range of optimum effective dosages, more difficulty is added to the problem where there is a lack of reliable

standardization. Some antigenic preparations are much more potent than others. Marked local or general reactions may be produced with comparatively small doses of some vaccines or only with large doses or more concentrated material with others. Mixed stock or autogenous respiratory vaccines are usually prepared from organisms such as streptococci, staphylococci, pneumococci, H. Influenza, M. Catarrhalis, etc., The organisms are killed or attenuated by heat or formaldahyde treatment. Then standardization is based upon the number of killed organisms per cc; this is usually 2,000 million per cc. This is not a very reliable standardization of potency. Some observers use the intradermal skin test as a measure of potency or of individual susceptibility or sensitivity. Serial dilution titration testing, by which the end point or weakest dilution which will produce a minimum positive reaction, may be of some value in determining potency or therapeutic dosage. A stock vaccine may be standardized clinically with some degree of accuracy by using it over an extended period of time on a large number of patients.

A trend toward the use of small doses of virus vaccines in which no reactions are produced is exemplified in the recent works of Salk and his associates.[7] They employed an emulsification of a large number of strains of influenzal viruses in light mineral oil. These vaccines were much more effective than similar aqueous preparations. It was found that there was no advantage in employing more than the quantity of virus necessary to achieve the maximum antibody level. High antibody levels lasted as long as four months.

Using the same technic of preparing emulsified vaccines, Salk[8] more recently has perfected a poliomyelitis virus vaccine which has been biologically tested on monkeys and which is now available in limited quantities for clinical trials.

Various bacterial toxins converted into the attentuated state as toxoids have been more effective on the whole than the standard killed bacterial preparations.

In general there is therefore a trend in the direction of the employment of attenuated live, yet still potent materials which are subjected to some form of biological standardization. Furthermore there is a trend towards the use of smaller doses not accompanied by reactions of any kind and doses which are maintained at an optimum effective level.

STAPHYLOCOCCUS TOXOID

Among the infections which are encountered in the field of otolaryngology, those caused by streptococci and staphylococci are the most important to be considered. Vaccine preparations of these two types of organisms have long been in use. A standardized toxoid preparation, however, has been available only for the staphylococcus. In some commercial preparations, staphylococcus toxoid is combined with staphylococcus vaccine. Streptococcus vacine may also be included in this combination. If a streptococcus vaccine is employed with staphylococcus toxoid the optimum range of effective dosage must be determined for each separately before being used in a combination.

At the present time we are concerned in the report of our observations on the use of staphylococcus toxoid only, rather than on a combination of vaccines and toxoids. On the basis of the use of staphylococcus toxoid over an extended period of time on a variety of clinical cases, we have been able to establish certain basic therapeutic principles of dosage which are also applicable to the employment of other vaccines and toxoids as well as to a variety of allergenic and pharmacologic agents (Fig. 4).

Staphylococcus toxoid has been used for the prophylactic treatment of recurrent boils, carbuncles, styes, and pustular acne since 1933. It has been suggested that the reactions noted in some cases indicate a hypersensitivity to staphylococcus proteins. The best results were noted in patients with a high sensitivity.

Standardization: Staphylococcus toxoid is prepared from a highly hemolytic strain of Staphylococcus aureus and is tested for its ability to stimulate antitoxin production. A unit of toxoid is the amount obtained from a dermonecrotizing unit of toxin (the least amount of toxin which by intradermal injection in a susceptible rabbit will produce an erythema, with a central necrosis at least 5 by 5 mm in diameter). Detoxification of the toxoid is effected with formaldehyde. It is carried to the point where the intradermal injection of 0.1 cc into the skin of the susceptible rabbit will no longer cause necrosis.

Tolerance Test: The manufacturers recommend a preliminary toxoid sensitivity test before the institution of treatment because in rare instances local and general reactions to 10 units (0.1 cc no. 1 dilution, 100 units per cubic centimenter) have been noted.

The sensitivity test is made by the intracutaneous injection of one unit (0.1 cc of a 1:10 dilution of Dilution 1). At the end of 24 hours the test is read and recorded as 1+, 2+, 3+, or 4+ according to the following results:

1+: Erythema less than 10 mm
2+: Erythema 10 to 15 mm
3+: Erythema over 15 mm without necrosis
4+: Over 15 mm with necrosis (rare)

Dosage: The initial dosage based on the above tests is as follows:

1+ reaction—0.10 cc Dil. 1 (100μ per cc) or 0.01 cc of Dil. 2 (1,000 μ per cc), (10 units)
2+ or 3+ reaction—0.10 cc of a 1:10 dilution of Dil. 1 (1 unit)
4+ reaction—0.10 cc of a 1:100 dilution of Dil. 1 (0.1 unit)

By this plan of treatment, injections are recommended by the subcutaneous or the intramuscular route and are given twice weekly. In general, the dosage is increased by 0.2 cc with each injection until the top dose of 1.0 cc of Dilution 2 (1,000 units) is reached. This usually requires about 10 injections. After the maximum dosage is established, the injections are given at weekly, sometimes at three to four week intervals.

In the above discussion, it was stated that the best results were obtained in patients with the highest degree of sensitivity. In these instances, very small doses were used. The initial dose was as small as 0.1 unit. In the treatment of furunculosis of the ear canal and styes, we noted very dramatic effects with doses of from 1/100 to 2/10 unit. These results suggest that the small optimum dosage is more satisfactory and that the build-up to the maximum tolerance of 1,000 units is unnecessary.

Metallergic Hypersensitiveness—The Anamnestic Reaction: In the use of staphylococcus toxoid injections we have noted that satisfactory responses may be obtained in certain allergic conditions, especially the allergic dermatoses as well as in a variety of bacterial infections with various organisms. In other words a non-specific effect may be obtained.

Urbach[9] refers to the term "metallergy" which was introduced to denote the fact that a specifically sensitized organism will respond to subsequent exposures of another type with specific allergic reactions presenting the same clinical picture as that elicited by the first allergen. The phenomena has also been called the "anamnestic reaction." For example, Mackenzie and Fruehbauer[10] have shown that rabbits sensitized to egg-white will after a while show no trace whatsoever of circulating antibodies to egg in their blood; these antibodies will reappear immediately, however, after the injection of typhoid vaccine. The same phenomenon has been noted in the use of bacteria instead of egg white. In an animal sensitized to a specific organism, antibodies could be made to reappear later following the injection of another different organism. This anamnestic effect is very strikingly reproduced by the therapeutic injection of staphylococcus toxoid. For example an ear canal infection caused by pseudomonas aeruginosa may respond very promptly to an optimum dose of staphylococcus toxoid.

It is generally known that in allergic individuals acute intercurrent infection (e.g. common cold, erysipelas) can for a while totally eliminate the allergic symptoms. The occurrence of a strictly specific shock of this type renders the organism temporarily incapable of reacting to other antigens. In other words an organism in combatting infection is not in a position at the time to create a sufficient number of antibodies to another antigen or allergen. With the appearance of the common head cold in an individual with nasal allergy the complete disappearance of the allergic process is exemplied by the total temporary replacement of eosinophiles by neutrophiles in the nasal secretions.

In the treatment of such allergic dermatoses as urticaria, infantile eczema and contact dermatitis we have been able to obtain very satisfactory responses often following the first injection of staphylococcus toxoid. So far we have not been able to reproduce such startling results in respiratory allergy. Failure to do so has probably been the result of not establishing the proper optimum dosage. The non-specific effects obtained in the treatment of allergic conditions with staphylococcus toxoid have been produced also by a variety of non-specific agents such as peptone, tuberculin, pyromen, milk, sulfur in oil, etc. Since staphylococcus toxoid is a standardized preparation it is a much more satisfactory material to employ because optimum effective doses can be more readily determined.

REPORTS ON USE OF STAPHYLOCOCCUS TOXOID IN OTOLARYNGOLGY

In 1941 Townsend[11] made a very comprehensive report of a group of 394 cases of acute recurrent rhinitis in which staphylococcus toxoid was employed in treatment. He used the skin test titration method to determine the size of the initial doses. From an analysis of the skin reactions, culture findings and results of treatment he noted that the patients appeared to be divided into two major groups:

Group I. (a) Frequent endemic head colds, (b) negative skin reactions, (c) staphylococcus albus (and aureus) predominant, (d) tolerant to increasing doses of staphylococcus toxoid, and (e) favorable results.

Group II. (a) Infrequent epidemic febrile throat and nose colds, (b) positive skin reactions, (c) occasionally staphylococcus aureus (streptococci predominant), (d) intolerant to increasing doses of staphylococcus toxoid, (e) unfavorable results.

On initial intracutaneous dose of three units (.03 of the No. 1 Dilution 100 units per cc) was used in the selection of cases for treatment. Townsend designated his method as that of the low dosage type, but the doses were low only in comparison to the massive ones usually employed. For example, he stated that the total dosage of 660 units in adults and 991 units in children was approximately one-fifth to one-tenth of the usual amounts of toxoid administered (3800 to 10,000 units). Of the entire group of 394 patients 193 were treated with toxoid. Sixty-five per cent had good results and 35 per cent had doubtful or unfavorable results. Of the cultures taken from the nose 66 per cent showed pure staphylococci. Of the 394 persons tested 63 per cent showed negative skin reactions.

As the result of his extensive studies Townsend stated that, "The cause of the different phenomena observed in different persons with the use of staphylococcus toxoid is unknown."

In the routine management of all cases of frequent and infrequent head colds it is of primary importance to determine whether the existing condition is infection or allergy. Sometimes the allergic patient has an acute infectious cold. The cytologic examination of the nasal secretions for the presence of neutrophiles or eosinophiles offers the only absolute method of making an accurate diagnosis.

In Townsend's series of cases no cytologic determinations were reported. It is evident therefore, that considerable difficulty was encountered in classifying the cases since no differentiation was made between infection and allergy.

Upon analysis of his two groups of cases it is reasonable to assume that Group I represented chiefly the allergy patients, because of the history of frequent colds, the predominance of staphylococcus albus which is usually a contaminant or a part of the natural flora, the tolerance to increasing doses of staphylococcus toxoid and the favorable results. In our experience allergic patients may have favorable results from the non-specific shock effect of the large doses.

The patients classified in Group II were quite evidently those with infections. As will be pointed out later patients with acute staphylococcus and streptococcus infections can tolerate only very small doses, for in this group the proper immunologic response to the infection must be obtained or the results will be unfavorable. If the dosages are even just slightly above the optimum level the infection is aggravated and the patient becomes worse instead of better.

In their report of clinical observations on the use of autogenous vaccine made from cultures of coagulase-positive hemolytic staphylococcus aureus Goodale and Mangiaracine,[12] a number of important points were emphasized in the treatment of bacterial infections of the eye and the respiratory tract. It was found that the production of coagulase was considered the best indicator of pathogenicity. Noncoagulase producers were considered as saprophytes or contaminants. Although staphylococci have been considered to be nonencapsulated in young (three-hour) rapidly-growing cultures capsules have been demonstrated. These organisms were thought to be preferable for the preparation of autogenous vaccines because of their greater antigenicity.

Although coagulase-positive hemolytic staphylococcus aureus is commonly prevalent in the nose and throat it is not pathogenic unless the balance between its virulence and the patient's immunity is upset in its favor. We are in agreement with Goodale and Mangiaracine that the antibiotics lower the resistance to bacterial infection. The occurrence of repeated respiratory infections in young children who had antibiotics for every acute episode is evidence to support this contention.

In their entire group of 113 cases representing various types of infection of the eye and respiratory tract Goodale and Mangiarcine reported that 88 or 78 per cent were definitely benefited by vaccine therapy

The initial dose of vaccine employed in treatment was .20 cc of a 1 to 100 dilution given intramuscularly. This was repeated on three successive days, then a rest period was allowed for four days. Following this same plan of weekly schedule the dosage was gradually increased until at the end of the fifth week 1 cc of undiluted vaccine was administered.

In the discussion of the above paper Fenton[13] suggested the use of low dosage but did not state the amount or the dilution employed. He suggested that most satisfactory cultures from the nose are obtained from the region above the posterior end of the middle turbinate.

Clerf[14] expressed the opinion that in vaccine therapy very small doses should be given. He further stated that the whole problem of immunity is the production of antibodies and the individual must have infection in order to develop them.

In the preparation of antogenous vaccines from the streptococcus and pneumococcus, Mangiaracine pointed out that it is almost impossible to stimulate antibody formation when using beta streptococci or pneumococci unless living cultures are used. More and more evidence is appearing in the recent literature to indicate that attenuated live bacterial and virus cultural materials are being employed in the preparation of vaccines with greater antibody production and with better therapeutic results.

PRINCIPLES OF SMALL OPTIMUM DOSAGE

The principles of an optimum effective dosage are based upon certain specific physiologic or immunologic responses. The responses follow a very definite pattern and apply to a great variety of antigenic and allergenic agents. Vaccine therapy based upon these principles was introduced long ago but the plan has been followed by only a few observers. In 1926 Crowe[15] reported his observations of the "Treatment of Chronic Arthritis and Rheumatism" in a small volume. In 1928 he opened the Charterhouse Rheumatism Clinic in South London. In a revision of his book in 1932 he[16] reported a

comprehensive summary of 662 cases. It was stated that between 80 and 90 per cent of the patients received benefit from vaccine therapy.

The vaccines used consisted of 157 strains of streptococci and two types of staphylococci (albus and aureus). They were made into a stock vaccine which was administered to this group of patients. The stock preparation was found to be more satisfactory than antogenous preparations. At first the initial dose was established at 500,000 organisms but on account of reactions it was reduced to 50,000. The smallest dose employed was 100 organisms. In some instances reactions were noted from this dosage but no attempt was made to reduce it further. Later, however, Small[17-18] who began his observations on the Crowe principle in 1927, reduced the dosages even below one organism. Since there was a limit for measuring dosages in terms of organisms, he began the use of bacterial extracts with which dosages were calculated on a weight-volume basis. His extracts were prepared according to the following plan: 1 - 10 dilution $= 10^{-1}$, 1 - 1000 $= 10^{-3}$ etc. In the treatment of rheumatoid arthritis doses as low as 10^{-16}, 10^{-15}, 10^{-14} were employed.

REACTIONS AND RESPONSES

The reactions and responses of small doses of various agents, especially Staphylococcus toxoid, which we have noted, correspond closely to those reported by Crowe and by Small in the use of bacterial extracts in the treatment of arthritis. There is a definite zone of dosage in which sharp exacerbations of symptoms follow the injection. This zone is just above the optimum or the effective one. We have noted, for example, that if one unit of Staphylococcus toxoid causes an exacerbation of a dermatitis, an urticaria, or an auricular furunculosis, a dosage of about 1/10 to 2/10 of a unit is followed by a satisfactory response. Acute exacerbations last only one or two days and may be followed by improvement. Dosages immediately above the reactive range become less pronounced in effect and with still higher amounts, no effect at all is produced. When very large doses are eventually administered, a general reaction manifested by lassitude, drowsiness, general aching, malaise, headache, anorexia and possibly a slight rise of temperature is produced. It is noteworthy that the larger of the microdoses, which do not produce evident reactions, are still much smaller than those generally employed in large dosage therapy (Fig. 4).

With micro—or minute dosage, a certain amount of a given dilution may cause a sharp exacerbation of symptoms, yet 100 times this amount may cause no apparent effect. Even repeated doses within this range produce no reactions. On the other hand, the one-hundredth part of this dose, which was followed by an exacerbation of symptoms, may upon repetition cause repeated flare-ups or reactions.

A dosage established below that which causes an exacerbation of symptoms is the amount which produces the optimum therapeutic effect. The relief of symptoms usually lasts only three to four days but upon repetition of the same dosage, the effect is repeated. As a rule, the length of the period of relief increases as treatment is continued. If the period of relief last only one to two days, or if the intervals of relief between injections do not eventually lengthen, then an increase in the dosage is indicated. If a focal reaction occurs on the same dosage then a reaction is indicated.

TECHNIC OF MICRODOSAGE

As will be pointed out later we learned that the effective dosage should be approached from the very weak ineffective zone to the one which produces the most satisfactory results, thus avoiding the zone of reaction. In other words, the zone of reaction should not be established first and then the dosage reduced below this.

Trial doses of he weakest dilutions may be given at three- to five-day intervals, increasing each five to tenfold until the zone of effectiveness is reached. It is not necessary to proceed with larger doses to produce a focal reaction; as a matter of fact, it is not advisable. If intermediate rather than the weakest doses are employed in the beginning, a dose which is too large may cause a marked exacerbation of symptoms lasting for several weeks, making it difficult to establish the effective dose. As a rule, a rest period should be allowed until the exacerbation has completely subsided and immunologic balance has become restored.

Analyses of Trial Injections: In the treatment of arthritis Crowe points out that four conditions may arise following a trial injection:

1. No change—Dosage too small.

2. Improvement—Beginning within a few hours after the injection. Pain, stiffness and swelling become less. In furunculosis of the ear canal, relief of pain often occurs also within a few hours. In these instances, the dosage is correct or nearly so.
3. The joints become worse within 24 hours. This represents a *focal reaction* and the dosage is too large.
4. The patient becomes worse—such symptoms as lassitude, drowsiness, general aching, etc., indicate a *general reaction*, consequently, the dosage is very much too large.

The plan of subsequent dosage may be summarized as follows:

Trial Injection No. 1 results in:	No change	Improvement	Focal Reaction	General Reaction
With Trial Injection No. 2:	Increase Dosage	Maintain Dosage	Reduce Dosage	Reduce Dosage Drastically

Focal and General Reactions: A very mild focal reaction lasting less than a few hours is not especially significant but would incate a slight reduction of dosage, say about 50 per cent. If the reaction lasts longer than 12 hours, the dosage should be reduced by ten times.

General reactions are of greater significance as the symptoms may last for several weeks. After the reaction has entirely subsided, it is advisable to start a trial dosage 100 to 1,000 times weaker. It is really more advisable to begin trial doses with the very weakest dilutions thus avoiding focal or general reactions. A focal reaction is more noticeable to the patient than a mild general reaction. The latter should not be overlooked.

Subsequent adjustment of Dosages: As pointed out repeatedly elsewhere, initial effective doses may be administered in chronic cases at three- to five-day intervals, later five to seven, ten, fourteen, twenty-one and twenty-eight-day intervals. If the intervals of relief do not gradually and progressively lengthen, the dosage may be increased by 50 per cent or more, but too much increase should not be made in an effort to establish a longer interval too early in the course of treatment. An exacerbation of symptoms may result. After injection intervals have been lengthened to three or four

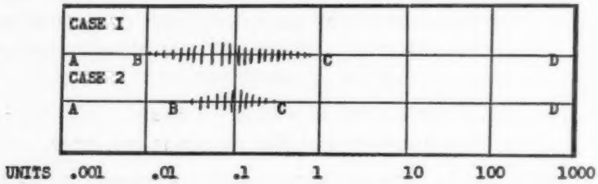

Fig. 1.—Ranges of reaction belt: Case 1 belt wide, Case 2 belt narrow.

weeks, further treatment may be discontinued but in some instances, may have to be continued for a year or longer.

In the use of this method of therapy it is important to learn the indications for manipulating the dosage. If the patient is showing satisfactory response the dosages must not be increased. It is usually advisable to try even a smaller dosage for in some instances we have noted that after several injections of the same amount there is a slight focal reaction. This indicates a reduction in dosage of about one-fifth.

Reaction Zones: The focal reaction zone below or above which no reactions occur varies in different individuals. The maximum is within 100, the minimum within ten times the increase above the effective range.

In Figure 1 the lines A B C D represent the entire range from ineffective dosage to general reaction. A B represents optimum effective dosage. B C represents the focal reaction range. The up and down movements of the broken line indicate the degree of reaction. Within this range note that the degree of reaction increases then decreases with increasing dosage, and that above C there is no reaction and incidentally no therapeutic effects. When very large doses are given such as near point D general reactions may be produced. Within this latter range there may be a nonspecific shock reaction with some therapeutic effect.

In case 1 the effective dosage lies between .001 units and about .01. The focal reaction range is from .01 units to 1 unit. In case 2 the effective range is below .05 units. The range of focal reaction is less than in case 1.

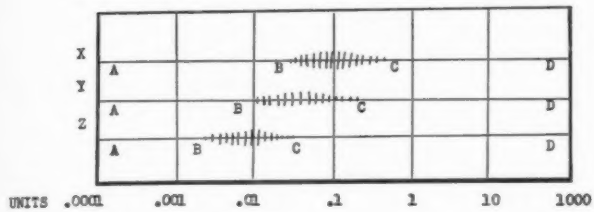

Fig. 2.—Change in range of dosage with prolonged therapy.

When treatment is extended over a prolonged period of time the range of effective dosage tends to decrease or shift to the left as shown in Fig. 2. X represents the situation at the beginning of treatment, Y after 2 to 6 weeks and Z after 6 weeks. If for example to top effective dosage is ½ unit at X, later it may drop to 1/10 unit and finally to 1/100 unit or less.

CLINICAL USE OF STAPHYLOCOCCUS TOXOID

When Staphylococcus toxoid was introduced in 1933 we used it in the treatment of furunculous of the ear canal but without satisfactory results. Further use was discontinued until about ten years ago when we discovered that certain small doses (1/10 to ½ unit) were effective in the treatment of urticaria. Later satisfactory results were noted in the treatment of various types of dermatitis such as infantile eczema, adult eczema and contact dermatitis. More recently we[3] found it effective in the treatment of the serum disease reactions following the administration of penicillin, such as urticaria, laryngeal edema, arthritis etc. The antiallergic effect of staphylococcus toxoid is non-specific as a variety of other bacterial and antigenic agents will produce the same effect. The evidence suggests that there is a stimulation of ACTH production.

Since small doses of Staphylococcus toxoid were effective in the treatment of allergic conditions, the application of this principle to the treatment of infections, such as furunculosis of the ear canal, hair follicle infections, in the vestibule of the nose etc. was found also to produce satisfactory results.[19-20] More recently it has been used in the treatment of acute respiratory infections with some instances of remarkable success (Fig. 3).

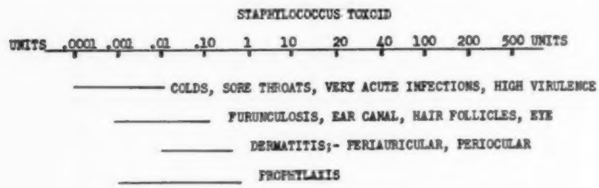

Fig. 3.

Respiratory Infections: Colds, sore throat, tonsillitis, acute sinusitis and bronchitis, serous otitis. For many years we have employed mixed respiratory vaccines in various weak dilutions for the treatment of these infections but the results were questionable and inconsistent, no doubt because of the lack of standardization of the materials and most important the failure to find the optimum range of effective dosage. More recently we began the use of staphylococcus toxoid employing the same dosages as established for furunculosis and for allergic conditions but no significant results were noted. Finally upon a more drastic reduction in doses by 10 to 100 times, definite immunologic responses were noted. More observations correlated with the bacteriologic findings and with invitro sensitivity tests must be carried out but the outlook in this field appears promising.

In some recent studies Tunevall[21] in Sweden investigated the behavior of certain respiratory infections in children at different ages. The behavior of the specific antibodies to such organisms as pneumococci, hemolytic streptococci, hemophilus influenzas, and pyogenic staphylococci were especially noted. Each of these organisms was found to have a predilection for a special age and it was noted that the antibody titers, as well as the ability to produce antibody in acute infections rose with increasing age. This development proceeded at different rates for different antibodies. Tunevall emphasizes the importance of these studies in the approach to the problems of the common infections in children at different ages. In 1949 ström[22] and his associates reported that in scarlatina, early antibiotic treatment greatly reduces the formation of antibodies. Tunevall does not advise the administration of antibodies for the milder respiratory infections but suggests that they be given in case of purulent complications.

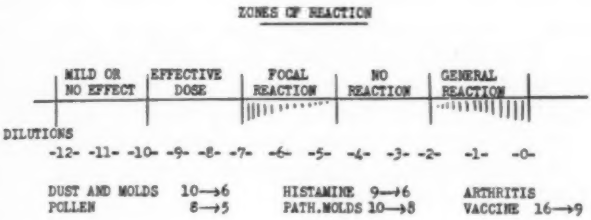

Fig. 4.

With the widespread use of antibodies today there is evidence that many of the respiratory tract infections are very much attenuated or less virulent than formerly encountered. There is apparently less antibody stimulation and less immunity produced. Following the use of antibiotics, antibody formation is further reduced. A knowledge of the proper use of bacterial vaccines to stimulate natural immunity and an abundance of antibodies is now a very timely problem.

In the administration of staphylococcus toxoid for respiratory and other infections we have noted that smaller doses (1/1000 to 1/100 units given every 3-4 days) are indicated with the more virulent infections. Further studies will probably show that vaccine dosage will have to be modified also according to whether it is employed before or after the use of antibiotics and according to the dosage of antibiotics administered. In some instances we have noted that the administration of Staphylococcus toxoid with a minimum of effective antibiotic dosage (250 to 500 mg of terramycin, acromycin, erythromycin or equivalent of other antibiotics) was followed by very satisfactory results.

Skin and Hair Follicle Infections: Since the Staphylococcus is a normal inhabitant of the skin, and since the skin is an important immunologic organ, maximum responses from the intradermal injection of optimum doses should be expected. In a group of 60 cases of furunculosis of the ear canal the response to vaccine and local treatment was noted within a few hours. In early cases the process was completely aborted. Pain was promptly relieved. In more advanced cases there was definite improvement and course of the disease

was shortened. By maintaining the injections at three to four day intervals until the infection had completely subsided there were no recurrences. The average beginning dose should be from 1/100 to 1/10 of a unit, varied according to the degree of acuteness of the infection, giving less for the more acute. In only two instances in 60 cases did we find it necessary to use antibiotics. Apparently the type of specific organism causing the infection did not modify the response to treatment with staphylococcus toxoid. Local treatment must be employed also as indicated.

In the treatment of hair follicle infections and infections of the skin of the vestibule of the nose, similar satisfactory results may be obtained. Seborrheic dermatitis or infection involving the canal and auricle as well as the eye brows which commonly spreads from the scalp promptly responds to toxoid therapy especially when combined with the use of Selsun (Abbott) shampoo on the scalp. In the eye with such conditions as styes, marginal blepharitis and conjunctivitis, responses to toxoid therapy also have been satisfactory.

Allergic Dermatitis: Dermatitis affecting the auricle and ear canal, the periauricular area, the periorbital region and adjoining parts of the face may be of the true atopic type, a contact dermatitis or a fungus allergy or infection (Candida albicans). The dermatitis may be complicated by secondary bacteria infection. The local application of Neocortef ointment is also advisable in most cases. Wet packs, lotions, ointments and powders are also used as indicated. Urticaria and angioedema may affect the various parts of the face, the lips, tongue, epiglottis, larynx and esophagus. The lesions may be localized or a part of a general reaction. In these cases the dosage of Staphylococcus toxoid varies from 1/100 to about 2/10 unit given intradermally at 3-4 day intervals (Fig. 3). In cases of fungus allergy or infection we have added the injection of an extract of a combination of Monilia, Trichophyton and epidermophyton in doses of .10 cc of 1 to 1 billion to 1-100,000,000. In general the doses should be gradually reduced if satisfactory results are to be maintained, thereby avoiding focal reactions because of a lowering of the threshold of tolerance.

Post-Antibiotic Complications: These complications consist chiefly of serum disease like reactions, fungus infections (Monilia), loss of normal flora of bacteria in the respiratory, gastro-intestinal and genito-urinary tracts, the development of infection of antibiotic

resistant organisms and the loss or reduction of normal bacterial immunity.

In the treatment of serum disease reactions, especially those caused by penicillin, manifested by urticaria, angioedema, generalized dermatitis, fever, joint pains etc. the response to Staphylococcus toxoid in doses of from 1/10 to 1/2 unit has been very striking. If toxoid administration alone is not satisfactory the administration of a short course (4-5 days) of ACTH and/or Cortisone therapy should produce prompt results.

The complications with monilial infection especially those observed on the tongue, cheeks, soft palate, tonsils, epiglottis, pharynx and esophagus respond to the injection of Staphylococcus toxoid combined with a monilial extract. The addition of injections of B-complex and the oral ingestion of acidophilis buttermilk or Lactinex Tablets and the avoidance of yeast containing foods such as bread, cheese, beer etc. should also be instituted.

The administration of Staphylococcus toxoid is also indicated in cases of infection with antibiotic resistant organisms especially with Staphylococci. Perhaps bacterial or virus vaccines should always be administered will all of the antibiotics. Certainly there is need for the restoration of natural bacterial immunity in these instances in which it is reduced from large doses or the repeated administration of antibiotics. It has been suggested that the antigenic stimulation of immunity by bacteria is absent when antibiotics with bacteriolytic properties are administered. And when bacteriostatic effects are produced the organisms are phagocytosed so very little if any antigenic material remains.

SUMMARY

1. Staphylococcus toxoid has proved to be of definite value in the treatment of certain infectious and allergic conditions encountered in otolaryngology such as: furunculosis of the ear canal and vestibule of the nose, seborrheic dermatitis of the auricles and face, acute respiratory infections, contact and atopic dermatitis of the auricle, periorbital area, nasal vestibule, urticaria and angioedema of the lips, tongue, pharynx and larynx; post-penicillin serum disease reactions and lowered immunity resulting from antibiotic administration.

2. The effectiveness of Staphylococcus toxoid is dependent upon the establishment and maintenance of an optimum small dosage.

3. Optimum dosage range is calculated upon the basis of certain immunologic responses. Effective doses were found to be below that which cause a focal reaction.

4. An increase or decrease in dosage is made only with the idea of maintaining the effective range.

5. No progressive build-up in dosage is recommended.

6. No general or constitutional reactions are encountered.

7. These principles of optimum dosage are applicable in the use of other bacterial or virus vaccines as well as a variety of other antigenic and allergenic agents.

8. The establishment or stimulation of natural immunity by use of vaccines should be employed in combatting infection in every instance in which it appears advisable, instead of giving antibiotics.

9. The antibiotics decrease the production of antibodies and lower natural immunity.

10. Combined vaccine therapy with minimum doses of antibiotics may be advisable.

11. Bacteriologic, immunologic and cytologic studies should be correlated with these therapeutic procedures.

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XXX

PRINCIPLES AND PROBLEMS IN SURGERY OF THE NECK

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It is presumptuous to undertake a discussion of neck surgery with the idea that we are dealing with a specific organ or system, such as we assume when we refer to stomach surgery, or genitourinary surgery. The neck is a corridor, an essential passageway between the head and face above, and the thorax and the rest of the body beyond. Surgery of the corridor is commonly undertaken for the correction or relief of conditions originating beyond its borders, and presupposes understanding of the pathological and anatomical problems of the adjacent areas.

The neck is really the province of many fields of surgery, of importance to many of the surgical specialties. The neurosurgeon is concerned with intracranial sepsis, vascular anomalies, cervical disc protrusions, and peripheral pain problems. The orthopedist also deals with disc protrusions, as well as torticollis, anatomic anomalies, and radiculitis. The plastic surgeon copes with the problems of contractures and scars, and other reconstructive problems. The endocrinologist presides over the vast field of thyroid and parathyroid disorders. The thoracic surgeon has long considered the adjacent neck as his own field, from phrenic nerve interruptions to esophageal reconstructions. Finally, the oral surgeon and laryngologist have a major interest in this area, not only in coping with direct problems of the corridor passageways, but in dealing with metastases from malignant neoplasms invading the cervical lymphatics. In summary, the neck is a common meeting ground for many surgical specialties, and the interrelations of the fields calls for frequent cooperative attacks on disease in the area.

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The basic requirement for neck surgery is a complete familiarity with the anatomy of the region. While this is prerequisite for all surgery, nowhere are important structures so closely crowded and interrelated as in the neck. The identification and preservation of anatomical structures demand a painstaking and fastidious technique. Hemostasis must be accurate and complete, adequate exposure must be secured by proper placement of incisions rather than by forcible retraction, and careful sharp dissection is preferable to blunt prodding and rooting to avoid accidental damage. It must be added that placement of incisions must also conform to the requirements of a cosmetically acceptable scar.

The necessity for complete anatomical knowledge and fastidious technique implies that neck surgery should be performed only by experienced surgeons. The training of residents and apprentices in this exacting field must be under the direct supervision of a surgeon completely familiar with the contemplated operation, and each step of a procedure must be planned and understood. Even the simplest operations may present pitfalls and lead to complications in the hands of the careless and unwary. For example, one of my medical colleagues collected a series of patients with spinal accessory nerve damage following cervical lymph node biopsy. In another instance, out-patient local excision of a node resulted in injury to a trunk of the branchial plexus. Numerous other examples could be cited, but it seems unnecessary to elaborate the point.

Granted a skilled and experienced surgeon, expert anesthesia is the next essential for good neck surgery. While many procedures may be performed under local infiltration or field block anesthesia, they become wearing and fatiguing for both patient and surgeon. We prefer a general anesthetic agent, with provision for maintaining a free airway, and for suction to remove secretions. Adequate oxygenation must be assured at all times. Intratracheal intubation with an inflatable cuff is most satisfactory. Tracheostomy should be performed without hesitation if it is desirable.

A basic principle of neck surgery has been to preserve intact those structures which serve as passageway for essential functions of the body. Classic operations of the neck therefore required preservation of the cervical cord and spine, the esophagus and trachea, and the vessels concerned with the blood supply of the brain. These restrictions imposed limitations on the scope of dissections, notably in

coping with malignant neoplasms in which primary or secondary involvement of some of these inviolable structures anatomically precluded a successful total eradication of the disease.

Modern advances in neck surgery have resulted in attempts to reappraise the inviolability of some of these structures, and to provide adequate alternative functioning pathways when the natural ones must be sacrificed.

I shall briefly consider some of these advances and their associated problems.

One of the first structures to be sacrificed with impunity was the internal jugular vein. This permitted control of the spread of infection, and opened the way to the development of the concept of radical neck dissection for malignant metastatic lymph nodes. There has been considerable experience with bilateral sacrifice of the internal jugulars, either simultaneously or in stages. This has been accomplished in numerous cases, but reports of disasters lead to the conclusion that the procedure is potentially dangerous or disastrous. A lumbar puncture needle connected with a manometer may permit some control of the sudden increase in intracranial pressure which follows occlusion of the vein.

Ligature of the common or internal carotid has long been recognized as dangerous and often fatal. When vascular anomalies are present, such as intracranial aneurysms or arteriovenous fistulas, collateral circulation may have developed which makes ligature safer. Procedures for gradual progressive occlusion over hours or days, as with a screw clamp, offer some promise of diminishing the dangers. Recently there have been explorations of free vessel grafts to replace sacrificed segments of the common and internal carotid vessels. Since the time of occlusion necessary to place a graft may in itself be long enough to cause brain damage, temporary by-pass plastic tubes may be helpful. Experimentally hypothermia during these operations appears to minimize cerebral damage.

Surgery of the pharynx has received great impetus since improvements in anesthesia and in the control of infection have controlled the prohibitive mortality and morbidity in this field. The discouraging radiation cure rate for malignant disease in this area has stimulated the operative approach. Reconstructions by flap grafts or free grafts around a mold or stent have been to some degree suc-

cesful. The swallowing function—passage of a bolus with protection of the airways from inhalation of food—is essential for the comfortable existence of the patient. In no field of surgery is it more important for the surgeon to evaluate his procedure not in terms of technical success but in terms of the increased span of comfortable or tolerable existence for the patient.

Radical surgery for carcinoma of the larynx is too firmly established to require discussion. While the voice is not an essential, vital function, there has always been a great reluctance to render a patient mute. The development of alternative pathways, either with the artificial larynx or preferably with esophageal voice, has permitted a freer and bolder attack on laryngeal cancer. Success with intrinsic carcinoma has encouraged operations for extrinsic carcinoma. The survival of large numbers of patients after laryngectomy has given time for the development of regional node metastases in many patients, and brings up the problem of regional lymph node dissections.

Neck dissection in the management of metastatic carcinoma of the cervical lymph nodes has been standardized for many years. Disagreements exist as to the indications for and the extent of dissection. In view of the high degree of error in clinical diagnosis of cervical lymph node metastases, we undertook some years ago a study to determine whether there are characteristics of the primary carcinoma correlating with the occurrence of lymph node involvement. In summary we found an increased occurrence of metastasis associated with longer duration, greater size, higher grades of malignancy, and invasive rather than proliferative mode of growth of the primary carcinoma. Recurrent cases, as opposed to those without previous treatment, presented a higher incidence of node involvement. These factors were of importance in varying degree in relation to all locations of primary carcinoma. There was marked difference between the sites of primary disease in the occurrence of metastases. In general, metastases were very common from primary carcinomas of the pharynx, extrinsic larynx, soft palate, tonsil and fauces; less common but frequent from the tongue and floor of the mouth; least common from the cheeks, lip, gingivae, intrinsic larynx and hard palate.

There has been some dispute as to the desirable extent of a neck dissection. Obviously, the objective is to remove all the nodes likely to be involved in metastases. While the anatomists have contributed greatly to an understanding of the normal lymphatic pathways of

drainage, their findings have been amplified and made concise by the clinical observations of numerous surgeons and pathologists. On the basis of our own experience we have considered a supraomohyoid dissection adequate to cope with metastases from most cases of carcinoma of the lips and cheek, reserving the radical dissection for the more malignant lesions of the tongue, floor of the mouth, soft palate and fauces, which drain directly into the deep cervical lymphatics.

The question of bilateral dissection arises for lesions encroaching upon the midline, and along with this, the decision as to whether both sides should be dissected at the same session. These questions must be solved for each individual case.

In recent years there has been a revival of employment of a one stage end bloc combined operation on mouth and neck, based upon the concept of the so-called "ideal" cancer operation which includes removal of the lymphatic vessels intervening between the primary focus and the regional node metastases. These operations are based on the assumption that the mode of lymphatic spread is by permeation, that is, a propagating thrombus of living cancer extending from from the primary disease to the involved node. While this mechanism may occur in some cases, especially in the late stages of the disease, the usual mechanism is embolic, and the intervening lymphatic vessels are free from involvement. Although the combined one stage operation is thus based on a false assumption, its employment has increased the scope of operation and the operability of many lesions, notably of the jaws, floor of mouth, base of the tongue, and the fauces. The increasingly radical nature of these operations has required development of reconstructive procedures by bone grafts and prostheses.

Another problem which arises in the neck is the appearance of a large node or nodes, demonstrated to be metastatic carcinoma by pathological examination, for which no primary carcinoma can be discovered. Frequently, repeated thorough examinations over a long period of time are necessary before an apparently insignificant primary carcinoma is discovered, usually at the base of the tongue or the pharynx. It is a tribute to the zeal and skill of our laryngological colleagues that there are fewer of these cases with undiscoverable sources now than there were twenty years ago. These cases used to be considered to be of branchiogenic origin, but many surgeons now doubt the existence of bronchiogenic carcinoma.

This brief summary has omitted many of the problems of neck surgery which are still under investigation even in the field of oral surgery and laryngology. Basically, all surgery of the neck requires recognition of the corridor function of the region, and must respect the anatomical and functional integrity of the passageways, or provide adequate substitutes for them. Viewed in this light, neck surgery is a broad field in which the possibilities for progress appear to be almost unlimited.

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XXXI

PHARYNGOESOPHAGEAL DIVERTICULUM AND THE OTOLARYNGOLOGIST

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The expanding field of otolaryngology has focused attention on conditions heretofore shared, in many instances, with the general surgeon. Pharyngoesophageal diverticulum is but one of these many conditions whose management rightly falls into the domain of the well trained otolaryngologist. Too frequently, articles on this subject have appeared in our journals stating that the otolaryngologist in the role of endoscopist is teamed with the general surgeon in the surgical correction of this condition. Except in those cases in which the diverticulum has invaded the thorax, the well trained otolaryngologist is thoroughly capable of performing this type of operation.

Attention was first called to esophageal diverticula in 1816 by Bell.[1] Zenker's[2] description of pharyngoesophageal diverticula in 1877 was so classic that the lesion is often referred to as Zenker's diverticulum. This presentation will be limited to a discussion of this latter type and a review of our experience with 73 cases encountered at the Ochsner Clinic in the ten year period ending December 31, 1953.

Contrary to indications in the literature, the incidence of pharyngoesophageal diverticula is not increasing but the diagnosis is merely being made with greater frequency. The condition is usually encountered in older people. The youngest patient in our series was 38 years of age and the oldest 78, the average age being 60.6 years. Probably the reason for this is that the patient may have the condition for years before it becomes troublesome enough to make him

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Presented at the meeting of the American Laryngological Association, May 28-29, 1954, in Boston.

seek medical attention. The lesion also seems to be somewhat more common in men than in women, 44 of our 73 patients being men.

Because of their location at the junction of the hypopharynx and esophagus, pharyngoesophageal diverticula are of great clinical interest to the otolaryngologist. They always occur on the posterior pharyngeal wall at the junction of the hypopharynx and the esophagus directly behind the cricoid cartilage where the oblique fibers of the inferior constrictor of the pharynx and the orbicular fibers of the cricopharyngeus muscle meet. In this location is a small triangular space, varying in size with the individual and unprotected by muscle. This area was first described by Lannier Hackerman and is frequently referred to by his name. A slight herniation develops in the posterior wall in the midline. As long as it is small, it will remain in the midline, but as it enlarges it will extend to one side or the other, usually to the left. In 46 of our patients the pharyngeal pouch deviated to the left side, 20 were in the midline and in only 7 was the deviation to the right side.

Because of no history of trauma or difficulty in deglutition, development of a diverticulum in this particular area is thought by some to be due to weakness of the triangular space between the muscle fibers. However, Jackson and Shallow[3] did not consider the theory of congenital weakness "a reasonable one." They believed the chief factor in their formation to be the pinchcock action of the cricopharyngeal muscle. The powerful action of this muscle keeps the mouth of the esophagus closed except when it momentarily opens to permit passage of food. If it fails to open, or opens tardily, such tremendous pressure is exerted in the walls of the hypopharynx that pouching may occur in a congenitally weak spot. This hereditary tendency to exceptional weakness in the posterior wall of the hypopharynx in four members of one family was recently reported by Bjork.[4] The association of pharyngoesophageal diverticula with goiter, which has been reported,[5] has not been observed by us.

Regardless of the etiology, once invagination begins, it gradually enlarges thereafter and the patient eventually becomes conscious of certain discomforts pathognomonic of this condition. The onset is so insidious that the patient may have symptoms for a long time before he seeks relief. On the other hand, some patients may have no manifestations to suggest the presence of the lesion. This was the case in nine of our patients, whose diverticula were discovered on

routine examination. Gradually, mild dysphagia and a sensation of fullness and choking develop, and the patient is bothered with unpredictable regurgitation, which usually seems to be more pronounced at night. Occasionally, patients will relate that they have a pocket in their throat, and pressure on the side of the neck results in regurgitation. Some patients complain of a sensation of smothering and an accumulation of fluids in the throat, particularly at night, which is frequently followed by severe bouts of coughing. Dysphagia progresses until loss of appetite and weight forces the patient to seek medical consultation. As the diverticulum increases in size and food accumulates within its lumen, the esophagus becomes more compressed and the patient becomes conscious of retrosternal pressure and discomfort. Gurgling noises are frequent and annoying.

Pharyngoesophageal diverticula may at times assume large proportions and retain food or fluids for a long time. Peikoff[6] reported the case of a patient who considered his diverticulum advantageous. He discovered that at cocktail parties the first few swallows of liquor lodged in the pouch, which distended considerably with each drink. Later in the evening, he could have an extra drink when he needed it by pressing the pouch with his thumb.

The diagnosis of pharyngoesophageal diverticula is easily suspected from the symptoms and quickly established by barium visualization of the esophagus. However, roentgenograms should be made in the anteroposterior and oblique positions. Esophagoscopy should verify the roentgenographic observations and eliminate the possibility of strictures or early malignancies. Esophagoscopy is not always easy; the location, size and pressure exerted by the diverticulum tends to push the esophageal opening anteriorly making it at times difficult to find and visualize satisfactorily. The mouth of the diverticulum remains open more or less at all times; hence food and liquids find their way into this sac more readily than into the esophagus proper.

The treatment of pharyngoesophageal diverticulum has long been recognized as essentially surgical, preferably in one stage, although some advocate two stage diverticulectomy in which the sac is first exteriorized and anchored in the wound near the skin, and ten to fourteen days later it is excised and the wound permitted to close by secondary intention. Welti[7] championed the two stage procedure because of its innocuousness, the tranquility it gives the

surgeon and the complete cure it provides. Knight,[8] on the other hand, is of the opinion that this method invites infection and other complications. Recently, Crile and Robnett[9] reported the successful treatment of pharyngoesophageal diverticula in 11 patients by employing the usual incision, dissecting up the neck of the sac, placing a purse-string suture around the neck and then inverting the sac into the esophagus. With modern asepsis and antibiotics this procedure would seem to have no particular merit. We have always employed the one stage operation because it is technically simple and gives excellent results. A physical examination determines the length of the preoperative hospitalization for rest, preparation and administration of fluids.

TECHNIQUE

An incision extending from the middle portion of the thyroid cartilage up to the clavicle is made along the anterior border of the sternocleidomastoid muscle, preferably on the left side except for diverticula located on the right side. The anterior border of the sternocleidomastoid muscle is retracted outward to expose the deep cervical fascia, which is divided parallel with the cutaneous incision. The carotid sheath and its contents are carefully retracted outward while the sternohyoid and larynx are retracted inward. If the omohyoid interferes too much with exposure of the sac, it may be divided. The thyroid vessels should be ligated. Exposure of the thyroid gland and rotation inward provide a view of the cricoid and adjacent tracheal rings. Posterior to these structures lies the esophagus, and if the sac is small, it will be found just below the level of the cricoid cartilage posterior to the esophagus. A large sac will be encountered before the esophagus proper is exposed. When the sac is found, it must be cautiously dissected free of its attachments. If any difficulty is experienced in localizing the sac, the esophagoscope is introduced directly into the diverticulum. Retained secretions are aspirated and a piece of merthiolated gauze to which a string has been attached, is packed into the diverticulum. Regardless of any difficulty, it has become routine for us to introduce an esophagoscope into the esophagus prior to excising the sac. This serves as a guide to excision of the neck of the sac. Before this was done routinely, too vigorous traction on the sac in two of our cases resulted in excessive removal of tissue, which in turn caused strictures necessitating dilation over a long period of time. When the sac is ready to be incised, the merthiolated gauze pack is removed perorally and the neck of the

sac is then carefully incised. Subcuticular interrupted sutures are used to approximate the edges of the delicate pharyngoesophageal mucosa and the muscular layers are carefully brought together and sutured tightly. A dermal drain is placed in the lower portion of the incision, and after the cervical structures are approximated, the wound is closed. A Levin feeding tube is used for four or five days.

RESULTS

In our series the 9 patients whose diverticula were discovered on routine examination refused surgical treatment. In spite of definite symptoms and large diverticula, 23 other patients were not operated upon. Nine of these latter patients had severe heart conditions making them poor surgical risks, several others were of advanced age and in poor physical condition and the remainder refused to undergo any type of operative procedure. Diverticulectomy in one stage under general anesthesia was done in the remaining 41 patients. Results were successful in 36 of these. Complications developed in the other 5 patients. Paralysis of the right recurrent nerve occurred in one; paralysis of the left recurrent nerve in another; a persistent fistula necessitating re-operation developed in the third patient and strictures necessitating prolonged dilatation developed in the other two patients but both eventually completely recovered.

COMMENT

Even though every precaution is taken to avoid injury to the inferior laryngeal nerves, occasionally such complications will occur resulting in paralysis of one vocal cord. This does not always mean that the nerve has been sectioned, as paralysis may result from traumatization of the nerve with forceps or from pinching of the nerve by scar tissue produced by postoperative infection. Also, infection may cause disruption of the line of sutures resulting in a fistula, which heals in due time. The two cases of stricture in the present series were due to removal of too much pharyngoesophageal mucosa which could have been avoided by insertion of an esophagoscope into the esophagus. Since doing this routinely, we have never removed too much mucosa. For this reason, we believe the esophagoscope should always be used in the performance of pharyngoesophageal diverticulectomy.

SUMMARY

Pharyngoesophageal diverticula are being recognized with increasing frequency. Because of their location at the junction of the hypopharynx and esophagus, they are of consciderable interest to otolaryngologists. They are thought by some to be due to congenital weakness of the triangular space between the muscle fibers and by others to the pinchcock action of the cricopharyngeal muscle. Patients become aware of the anomaly by gradual development of dysphagia, a sensation of fullness and choking and unpredictable regurgitation. These clinical manifestations suggest the diagnosis, which may be readily established by barium visualization of the esophagus. Treatment is surgical excision of the diverticulum, preferably in one stage. Of 41 patients with pharyngoesophageal diverticula treated in this way, successful results were obtained in 36; complications developed in the remaining 5.

Because of the exposure to excellent training in neck surgery, and because of the intimate knowledge and daily experience with the pharynx, hypopharynx, larynx and esophagus as well as with cervical anatomy, the otolaryngologist occupies an enviable position when surgical correction of pharyngo-esophageal diverticula is considered.

OCHSNER CLINIC.

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XXXII

TREATMENT OF MAXILLARY TUMORS THROUGH THE FERGUSSON EXTERNAL APPROACH

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and

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(By Invitation)

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This paper considers the surgical approach to tumors of the maxilla, and is not intended as a general review of methods of treatment of maxillary tumors. That subject with comments on recovery rates and prognosis has been reviewed by others.[1-6] This paper deals only with the mechanical approach to the maxilla; its purpose is to call attention to the Fergusson incision, to review the history of that incision, to compare it with others used for the same purpose, and finally to present a few illustrative cases.[7,8] Rather than write lengthy case reports to present a few salient points, these points are elucidated in the captions beneath the photographs which accompany the paper.

The Fergusson incision consists of two arms placed at right angles to each other (Figs. 1 to 4). The vertical arm lies in the groove between the nose and cheek, goes around the nasal ala and under the naris on the same side and finishes by going straight down from the midline of the columnella cutting completely through the lip. The second arm is horizontal lying under the eye and joining the vertical portion at its upper end. In actual practice one can start this incision at either end, and usually does not make the two arms separately. The horizontal arm under the eye is placed in a skin fold if possible. The vertical arm is placed in the groove between nose and cheek. One must divide the soft tissues clear through to the bone and the authors have used sharp dissection for this division. Using the

From the Division of Otolaryngology of the University of Minnesota Medical School.

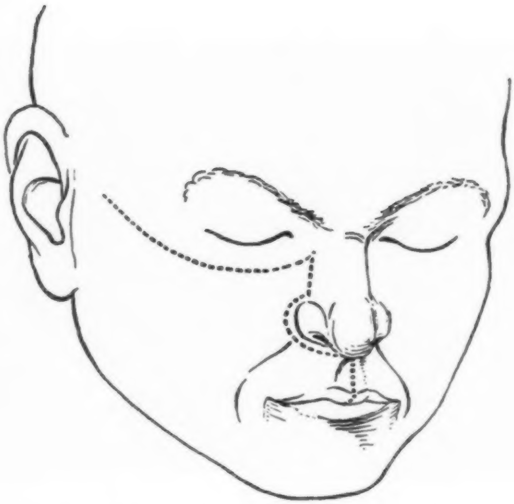

Fig. 1.—Diagram showing external limits of Fergusson incision. (From Tumors of the Head and Neck by Ward and Hendricks, Williams and Wilkins publishers, Baltimore, 1950, see bibliographic reference.[8])

electric knife would make this much easier because it would control most small bleeding vessels immediately. To the authors it seems disadvantageous because it does not permit the recognition of abnormal tissue with the ease that exists when one uses sharp dissection. After one has accomplished the division of the soft tissues down to the bone, and has secured hemostasis, he is ready to reflect the flap laterally to expose the maxilla. The cheek is very vascular and one must allow himself considerable time for the making of the incision and the securing of hemostasis; he must put on many clamps, cauterize or tie the vessels, and then do the whole thing over again perhaps three times before he gets through the tissues of the cheek down to the bone itself.

The reflection of the cheek off of the maxilla can be done with sharp or electric dissection. Again the authors have the same objection to electrocoagulation voiced previously. Speed can be a disadvantage if it prevents recognition of neoplastic tissue. One picks up the cut lip and makes a horizontal incision in the mucous membrane similar

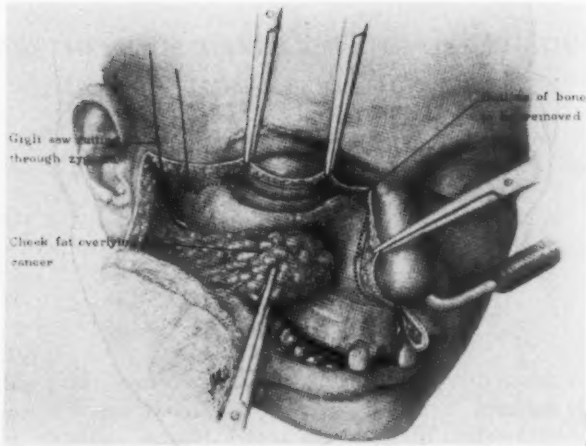

Fig. 2.—Operation for resection of superior maxilla, cheek flap turned back showing growth perforating anterior antral wall and involving subcutaneous fat. Note lines of bone incisions through the midline of the upper jaw to the floor of the nose across nasal bone and through the zygomatic arch and lateral antral wall. (From Tumors of the Head and Neck by Ward and Hendricks, Williams and Wilkins publishers, Baltimore, 1950, see bibliographic reference.[8])

to that of a Caldwell-Luc incision but extending to the midline. This liberates the lower end of the flap. Then one gradually accomplishes the lateral reflection securing his blood vessels as he goes. When one has completed the lateral reflection of the soft tissues the midline of the lip on the diseased side lies adjacent to the ear. The blood supply of this flap is secured through the external maxillary artery. One divides the infraorbital nerve end artery where they come out of the infraorbital foramen. As the reader will see when he inspects the picture taken from Fergusson's book this is exactly the opposite of Fergusson's original principle (Fig. 5). In his original flap the blood supply came from the infraorbital artery and the external maxillary artery was cut.

One then proceeds to remove the maxillary bone. Using a mouth gag of the Crowe-Davis type to expose the roof of the mouth,

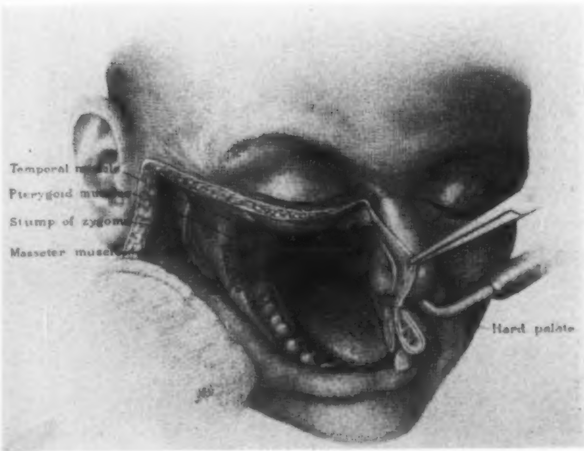

Fig. 3.—Superior maxilla has been resected. Hemostasis secured. (From Tumors of the Head and Neck by Ward and Hendricks, Williams and Wilkins publishers, Baltimore, 1950, see bibliographic reference.[8])

and having removed the first incisor tooth on the diseased side, if it is present, the electric knife is used to divide the soft tissues on the roof of the mouth back as far as the posterior edge of the maxilla; this incision is then carried laterally behind the posterior end of the processus alveolaris of the maxilla. Next, using mallet and osteotome, the maxilla is cut free along the side of the nasal bone upward from the nasal aperture, and laterally under the eye leaving the infraorbital ridge if possible, then downward either medial to or lateral to the front end of the zygomatic arch depending upon the extent of the disease. Even if the external carotid artery has been ligated there will be considerable bleeding when the maxilla is detached and removed. It is our custom to ligate the external carotid artery, and it seems reasonable that there is less bleeding than with the artery intact. However, there are people who think that ligation of the artery is not useful.

In preparation for the surgery the extent of the tumor has been estimated as accurately as possible. It is our custom to prepare draw-

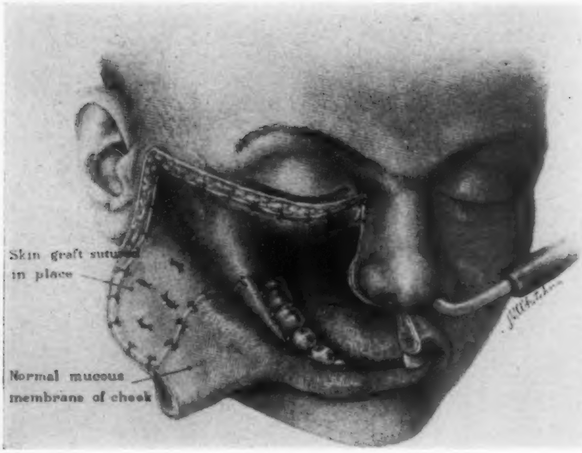

Fig. 4.—Split-thickness graft sutured over all raw surfaces of the cheek, masseter muscle, and pterygoid fossa. Wound closed. (From Tumors of the Head and Neck by Ward and Hendricks, Williams and Wilkins publishers, Baltimore, 1950, see bibliographic reference.[8])

ings of the area expected to be exposed. The drawings are numbered at points around the periphery of the area where biopsies may need to be taken. Twenty or so small containers are labeled and sterilized for the various biopsies. The tumor is removed grossly until one thinks that he has completely eradicated it. Biopsies are then taken from the periphery of the wound and frozen sections are made immediately. If tumor is found in the frozen sections one then goes beyond the original periphery of the wound and removes further tissue and makes second biopsies. It is convenient to number the first biopsy with the Arabic digit and the second biopsy from the same site with the same digit followed by the letter, A, B or C depending upon whether one is dealing with the second, third or fourth biopsy from the same site. Thus the first biopsy might be numbered 2; the second biopsy from the same site but further out from the center of the excised area would be numbered 2A; and if 2A proved to contain tumor the third biopsy would be numbered 2B. When all biopsies are free from tumor on frozen section, if one is

Fig. 5.—Incision used for "Removal of a Tumor of the Maxilla in a Woman." (From Ferguson, "A System of Practical Surgery," published 1845, page 530, see bibliographic reference.[7])

fortunate enough to be able to accomplish this, it has been our custom to coagulate the wound thoroughly all over with the electrocoagulating current. This results in sequestration of bone later because the bone is devitalized and undoubtedly destroys some occult tumor tissue. The wound is packed with gauze impregnated with petrolatum, and the large flap of cheek is brought back and carefully sutured into its normal position. It is necessary to unite the subcutaneous tissues very thoroughly so that minimal tension will exist on the skin sutures. It is necessary to be particularly careful in the apposition of the lip. One should make this union very strong and one should be very careful to appose the two points of the cut vermillion border of the lip with great delicacy. The use of a feeding tube postoperatively for a few days is desirable.

Removal of the packing from the cavity is done several days after the operation. Usually we have reanesthetized the patient, introduced an endotracheal breathing tube and packed off the pharynx just as we did for the first operation. Then we have removed the packing carefully. By the time one is ready to remove the packing, the permanent paraffin microscopic sections of the tissue examined by frozen section at the time of operation have been prepared. Be-

Fig. 6.—(Left) Photograph of a male patient three months after a right-sided Fergusson incision for carcinoma of the maxilla. In this case the entire maxilla including the infraorbital ridge, and the floor of the orbit was removed.

This patient illustrates two complications. He has the marked edema of the lower eyelid present in most of these patients but which, in our experience, subsides after approximately six months. He has a second complication in the form of a breakdown of the incision through his lip. This was the result of inadequate surgical repair, plus the pull of a very strong orbicularis oris muscle, plus trauma due to an attempt to get a denture into the mouth before the incision had a chance to heal. Secondary repair of the lip has been carried out since this photograph was made and the result is satisfactory.

Fig. 7.—(Right) Photograph of a male patient aged fifty years who was two and one-half years post-operative at the time this picture was made. The patient had a moderately low-grade carcinoma situated in the lower portion of his antrum and one which should be favorable for ultimate cure. Right maxilla was totally removed except for zygomatic arch using incision and procedures illustrated in Figures 1 through 4.

Fig. 8.—Photograph of a forty-four year old male eight months postoperative after removal of the left maxilla because of a cylindroma. Frozen sections showed tumor tissue high up in the antrum on the anterior wall, although all other indications seemed to show complete removal of the tumor. We feel that this man stands a much better chance of cure because of the accuracy with which frozen sections, made from tissue removed high up in the antrum, could be utilized to delimit the outer margins of the tumor.

cause the pathologist can be more accurate with these sections than with the frozen sections, one may have learned that some areas which appeared to contain no tumor when the frozen sections were made, in fact did contain tumor. By removing the packing under general anesthesia one can cauterize these areas further, or even do secondary removal of tissue at this time. Furthermore removal of the packing under anesthesia is a humane procedure compared with doing it without anesthesia. It is easier on the surgeon as well as on the patient. It is safer because it allows command of the situation if there is significant bleeding from any point within the operative cavity.

Patients who have had the Ferguson incision made have all of the usual difficulties following maxillectomy. The cavities crust a good deal and the odor is fairly unpleasant and strong. If the patient is sensitive it is necessary to build up his morale and self-confidence by constant reassurance and by insisting that his family help him in

this regard. The patient may need narcotic drugs at first after the operation and may become dependent upon them. Sometimes rather heroic measures are necessary to get the patient to be dependent upon himself and not upon the drugs. It is common to have very marked edema under the eye above the horizontal arm of the incision (Fig. 6). One evidently interrupts the venous return from the lower eyelid and a large quantity of fluid is imprisoned in the lid. In our experience this condition has corrected itself about six months after the operation. At times it has been necessary to support the edematous lower lid using a piece of adhesive tape fastened to the cheek above the outer canthus of the eye to form a sling. This has prevented the lower lid from being pulled away from the lower half of the ocular globe with resulting conjunctival irritation. It is possible that the tension of the cheek muscles, and sometimes the manipulation of the dentist in making the prosthesis may disrupt the suture line in the midline of the lip (Fig. 6). This may necessitate secondary repair. In the authors' opinion all of these things are of no great significance when one considers that he has had an adequate opportunity to remove the tumor for which the operation was done in the first place. The final cosmetic results certainly bear out this attitude (Fig. 7 and 8). This author believes that the adequate visualization of the maxilla afforded by this incision far outweighs any disadvantages the incision may have from a cosmetic standpoint.

The history of the Fergusson incision will now be examined. In 1845 William Fergusson described an operation for removal of a tumor of the maxilla in a woman.[7] He said that the tumor was, "Fortunately of a hard description, more in fact like an exostosis than what is usually called osteosarcoma, and although firmly fixed, in consequence of the thickened state of the surrounding processes of bone, was successfully dislodged and months afterwards the girl's appearance was as represented in the other likeness" (Fig. 5). He then said, "Operations for the removal of tumors connected with the upper jaw are by no means so modern as some seem to imagine. Such a proceeding is said to have been accomplished as far back as the seventeenth century." He then discusses several cases of tumors of the maxilla and finally says, "Dupuytren claimed to be the first to propose and execute this operation but beyond a doubt it was first performed in this country (England) by Mr. Lizarres in 1826."

As the reader will see by inspection of the pictures taken from Fergusson's original work he made two incisions, one like the modern

incision often named the "Moure" and a second one extending from the region of the zygoma down to the upper lip just medial to the outer corner of the mouth.. As pointed out earlier in this paper, these incisions would leave the flap with only the blood supply from the infraorbital artery and would necessitate division of the external maxillary artery. In fact, Fergusson describes division of this artery in detail in his book. Thus the incision carrying the name "Fergusson's incision" today is in fact not the same incision as that described by Fergusson in 1845. Furthermore Fergusson himself makes very plain the fact that he claims no originality for the incision and that it probably antedates him by a considerable period. However when one acquaints himself with Fergusson's life and accomplishments he is only too happy to see the perpetuation of Fergusson's name, even though there may be some slight inaccuracy in its application.

Sir William Fergusson (1808-1877) of Prestonpans, Scotland is said by Garrison to be the founder of conservative surgery, that is, of the preservation of parts of the body which were needlessly sacrificed by earlier operators.[9] Before Fergusson's time, denuded bones, diseased and painful (even neurotic) joints were regarded as sufficient reason for amputation. Fergusson held it to be "A grand thing when by prescience even the tip of a thumb can be saved." Fergusson's progress in substituting excision for amputations was rapid after he began his practice. His surgical experience was large. Between 1828 and 1864 he is reported to have operated four hundred times for hare lip, with only three failures and one hundred and thirty-four times for cleft palate with one hundred twenty-nine successful cases. He proceeded with such lightening speed and skill that a visitor was advised, "Look sharp for if you only wink, you'll miss the operation altogether." Fergusson is said to have been an indifferent lecturer but beloved by his patients and adored by children. He was highly accomplished, a good violinist, an inventor of many surgical instruments, so expert in carpentry and metal work that he could devise any necessary apparatus out of hand, an enthusiast at fly fishing and at dancing the Scottish reel. He was noted for his great generosity and hospitality to struggling authors and dramatists, and medical students.

The incision which today goes under the name of "Moure's" consists of the vertical arm of the Fergusson incision with certain

minor modifications.[10] The basic Moure incision is carried along the nose and the cheek and encircles the ala and runs beneath the naris. It may include an extension to cut the lip in the midline, and a second extension going up medial to the inner canthus and ending in the eyebrow. Thompson and Negus say, "It is never necessary to make a second incision curving outward below the orbit."[10] Ohngren makes the midline incision in the lip extending it into the naris.[6] He then retracts the lip and makes an incision around the pyriform aperture somewhat in the same position as that which would encircle the alar cartilage if it were made through the skin, and a second incision along the maxilla through the mucosa in the gingival fold over the canine fossa somewhat in the manner of the Caldwell-Luc incision. No doubt there are many other modifications of these incisions which have not come to the attention of these authors.

It would seem that the Fergusson incision is indicated in cases of maxillary tumor in which the overlying skin and soft tissues are not likely to be invaded by the tumor to a degree requiring their excision, and to cases in which paramount importance is attached to the ability of the operator to visualize the entire maxillary cavity during removal of the maxillary tumor. It is the authors' opinion that this set of conditions exists in a great many maxillary tumors, with the exception of the very smallest ones located in extremely accessible positions. If one wants to give his patient the best opportunity for cure in any maxillary tumor he must be able to make adequate visual examination of all parts of the maxilla. It seems that this can be accomplished very well through the Fergusson incision and we believe that it can be accomplished better through this incision than the others described. Furthermore it is easy to do lateral rhinotomy and to excise the zygomatic arch if this proves to be necessary. In our cases illustrated herewith, it seemed to us that we gave out patients better chances for recovery because of our ability to make frozen sections high up in the antrum with the degree of accuracy made possible by the very adequate exposure permitted by this incision.

SUMMARY

This paper describes the performance of maxillectomy through the Fergusson incision using frozen sections as a guide the extent of removal necessary. The history of the incision is reviewed by examination of Fergusson's own writings. The incision is compared to

others used for maxillectomy. Complications and good results are illustrated with photographs.

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(Scientific papers of the American Laryngological Association to be continued.)

The Scientific Papers of the American Otological Society

XXXIII

ADDRESS OF THE PRESIDENT

FREDERICK T. HILL, M.D.

WATERVILLE, ME.

I am deeply appreciative of the privilege of serving as President of the American Otological Society, indeed a great honor.

Custom calls for an address from the presiding officer to open each Annual Meeting. With some misgivings I have chosen to discuss certain relations, possible problems of our specialty, which might seem pertinent at this time. I shall endeavor to do this as objectively as possible.

It is not my intention to preach a sermon, yet I have selected a text, one of the wise sayings of my teacher, my friend and always my chief. Like many other great physicians Dr. Harris P. Mosher has coined many an aphorism which will live long after him. The one I have chosen, my text, if you please, is:—"The strength of Specialism is Specialism and, paradoxically, the weakness of Specialism is Specialism."

Otology is one of the oldest of the medical specialties. From its early beginnings it has been characterized by an inquisitive attitude, fostering investigations as to the nature of hearing, the mode of transmission and of interpretation of sound. Speculative theory, often surprisingly correct, far antedated the development of facilities for accurate investigative techniques. This Society may well point with pride to its research program, to its efforts in the conservation of hearing and its interest in rehabilitation of the deafened. As a result of these and allied programs, as well as advances in medicine

From Thayer Hospital.

generally, we find a rather definite shift in our objectives which becomes reflected in a somewhat different type of clinical practice. Emphasis has been shifted from the management of acute surgical emergencies, which once occupied a major portion of the otologist's attention, to other conditions, equally important but previously rather neglected. While life-saving procedures still constitute an important and necessary part of our practice, more and more we have become concerned with the preservation of function and with rehabilitation. Otology has become a changed specialty, yet an expanded one. If, as we sincerely believe, it has become a stronger one, what may be its weaknesses, inherent in these new developments?

While advances in therapy have resulted in a lessened incidence of surgical mastoiditis and its complications, it has brought about a change in the clinical picture of this condition. Apropros of this let me quote from Dr. Mosher: "Nature does not tell you when to operate as she used to do. The masking effects of the "sulpha" drugs and the antibiotics call for more clear thinking and more mature judgment on the part of the surgeon than of old. The precept—When in doubt do an exploratory operation is now doubly true."

Surgery of the temporal bone has made distinct advances, due largely to the work of Sourdeille, Holmgren and Lempert. It is hardly necessary to point to the technical developments made by the last named, often in the face of seemingly unsurmountable handicaps, which resulted in the perfection of the fenestration operation. The great value of this procedure, in properly selected cases, is indisputable. It would seem, however, that generally, interest has been focused upon techniques. But now, with the technical problems largely solved, we see emphasis shifting to the importance of better appreciation of the prognosis in the individual case.

Hilger, three years ago, called attention to the changing character of our specialty, stating that the otologist no longer was "just a temporal bone carpenter or a tubal piddler." While this somewhat caustic reference to the past may seem an unjust criticism of those who laid the foundations of otology, the main contention is a correct one; that our field is changing and our horizon is broadened; and we must recognize this and become prepared to meet the responsibilities of this larger field.

As otology has expanded, taking a broader prospective of the patient as a whole, we must not lose sight of a similar expansion in

other fields of medicine, with added skills becoming more generally available. As our wider horizon indicates a strengthened otology, may it possibly develop a weakness through a feeling of self-sufficiency, in failing to make use of all indicated skills, at least in a consultive capacity?

The work of many investigators, including Furstenberg, Lathrop, Cawthorne, Day, Lindsay, Williams and Hilger, of this Society, has given us a better understanding of Ménière's disease and a broader insight into the problems of the vertigenous patient. While we are better able to cope intelligently with this situation as a result of these studies, I wonder if our therapeutic approach, is always as effective as it could be. The fundamental imbalance of the autonomic nervous system, the significance of the stress factor and the probability of a functional overlay makes a purely otological approach often inadequate. Personally I have felt far safer in working in close conjunction with an internist skilled in the diagnosis and management of vascular disease. I cannot view this condition as isolated within the vascular bed of the internal ear. The clinical manifestations may be so localized, but an over-all approach to the problem would seem to offer decided advantages. In other words this well may be a problem for team work, including the internist, the otologist, and at times the psychiatrist.

Not infrequently we face problems which are intimately related and anatomically adjacent to the fields of neurology. While I recognize that many otologists, members of this Society, by training and experience, are eminently qualified in neuro-otology, by no means can this be said of the men in our specialty as a whole. Many of us have been accustomed to dealing with brain abscess, diagnostically and surgically, but would we not strengthen our position by at least consultation with the neurological surgeon?

Acoustic neuroma often is, or should be, first discovered by the otologist, but few, if any of us, would feel confident in making a definite diagnosis without neurological confirmation.

Indeed should not most cases of impaired hearing receive the benefit of medical consultation? Is it enough that we search our own field for evidence of excessive lymphoid tissue, infected sinuses, or altered air currents in the nose, to the exclusion of other possible significant conditions better handled by the internist, the endocrinologist, or the pediatrician?

The history should point the way, leading toward the logical course to be followed. A good history cannot be hurried. It is very liable to be time-consuming. In a busy practice there may be a temptation to hurry through this procedure, with the patient in the examining chair, and the doctor standing by, seemingly impatient to get on with his examination. Such a history often fails of its purpose and results in the physician missing valuable clues, indicating diagnostic aids and consultations which would be beneficial.

Sometime ago I had occasion to refer a patient to an internist who had recently joined our group. He was a well-trained and experienced man in his specialty. The patient had been referred to me with a diagnosis of Ménière's disease. She did not meet my diagnostic criteria and the history strongly indicated a vascular background with carotid body involvement. When I gave the internist the history I had taken, I was both surprised and hurt by his comment: "I never knew before that an ear, nose, and throat man took a real history." I feel that this criticism of our specialty is not justified as a whole but yet there must have been grounds for it in certain of the doctor's past experiences. This often may be a weakness attributable to and inherent in too busy a practice.

The American Otological Society, in developing its research program recognized from the first the necessity for a broad program encompassing many different fields of scientific investigation. While it initial project was the study of the factors involved in otosclerosis, the scope of the work gradually expanded as the entire problem of deafness came under scrutiny. The development of the audiometer initiated the inclusion of electronics in our investigative armamentarium, and the work of Wever and Bray brought the biophysicist into the picture. Gradually as our sights were lifted and our horizons broadened, conservation and rehabilitation began to receive attention. All of this led inevitably to the birth of a specialty within a specialty, namely audiology.

Audiology, of course, is the science of hearing. As such, what of its relations with otology? Once in a facetious moment I called it "Ph.D. Otology." Few otologists pretend to any but the most superficial knowledge of acoustics; and I would doubt more than a speaking acquaintance on the part of the audiologist with clinical otology. Consequently the importance of cooperation is obvious, not alone in research but in the development of programs of conservation

and rehabilitation. We are all familiar with numerous examples, largely in university centers, whose activities indicate a broadened specialty. Unfortunately, there are instances when the designation of audiologist has been rather loosely applied or even abused, an added reason for the cooperation of the otologist and the truly qualified worker in audiology.

Our rather belated interest in the rehabilitation of the deafened allowed an unfortunate situation to develop. For years otologists generally took little interest in providing amplification for patients who might be benefited thereby. Hearing aids were left almost exclusively in the hands of dealers. While much has been accomplished by the Council on Physical Medicine and Rehabilitation of the American Medical Association in setting up standards of performance and in designating those hearing aids found acceptable, we are all too cognizant of the wide-spread solicitation of potential purchasers and the high-pressure salesmanship sometimes exercised to sell or replace hearing aids. If possible, these people, handicapped by impaired hearing, should be protected from exploitation. The solution would seem to be in the further development of hearing aid centers. In addition to those already available, facilities might well be set up in all hospitals having departments of otology. This would necessitate otologists generally taking a greater interest in this problem. Such a program surely would strengthen our specialty and prove a boon to many people, handicapped by impaired hearing.

I cannot close without commenting upon something not particularly germane to our specialty but which is of importance to the practice of medicine. I refer to certain problems in relation to our hospitals. And as a segment of the medical profession we are not immune to these problems nor should we be indifferent to them. Perhaps I have been made cognizant of them because of certain administrative responsibilities in the work of the hospital associations.

Modern medicine is irrevocably associated with the hospital. What once might have been a marriage of convenience, now has become one of necessity. Our hospitals, perhaps more than any other of our social institutions, are called upon to meet the challenge of a changing economy with rising costs on all sides and a diminishing supply of personnel, due largely to inability to meet the competition of industry and of government. And our hospitals must supply one quality of service, only the best, to a market that often is hard-

pressed or unable to meet even the cost of such service. Yet it must do so if we are to preserve our system of medical practice.

Not a little of the difficulties faced by our hospitals can be attributed to a failure of cooperation, indifference, or lack of understanding upon the part of members of our own profession. One of the glaring omissions in our program of medical education has been the failure to include courses aimed at acquainting the young physician with the actual operation of the hospital, the place in which he, later, will spend approximately two-thirds of his working time. The interne or resident leaves the hospital with an adequate training in clinical medicine but with little or no comprehension of the multiplicity of factors involved in its operation. Too often this is all taken for granted. Some indoctrination into the objectives, the philosophy and the problems of the hospital would do much to dispel the misunderstanding, even antagonisms, which can be so detrimental both to hospital and staff.

For example: What does the average physician know about the cost of caring for a patient in his hospital? About the necessity of conserving the time of personnel to provide services which are both economical and efficient? About the importance of planning admissions and scheduling operations so as to spread the patient load most efficiently and at the same time provide the best of nursing care? About signing discharges promptly so that the admitting office may know what accommodations shortly may be available?

Therapeusis, today, has become both elaborate and expensive, often very expensive. Excessive and unnecessary use of various drugs, often some proprietary pet of the physician, is a common cause of high costs of patient care, reflected in the patient's bill and many times necessarily absorbed by the hospital. No hospital desires to restrict the physician's efforts to provide his patient with whatever may be needed by way of treatment; yet, except in rare instances, adherence to a well-planned hospital formulary would be quite efficacious and do much to cut down costs.

In a paper read before the American Broncho-Esophagological Association in San Francisco in 1950, Dr. Bloomfield said that there was a type of practice prevalent in our hospitals today which was especially common with residents and internes. When a patient was admitted the physician proceeded to order every conceivable laboratory test which he could think of, in the hope that some of them

might provide the answer and make it unnecessary to exercise his own mental powers of deduction. He called this "peripheral medicine." This is an apt designation, much more so than the tag so frequently applied, of scientific medicine. It may be scientific if that implies laboratory mechanics in place of mental activity, but it also means expensive medicine, for somebody has to pay for it; if not the patient, then it comes out of the funds of the hospital. Another cause of the high cost of hospital care!

The Blue Cross plans have been the salvation of the majority of our voluntary hospitals but, today, their solvency is jeopardized by the abuse of benefits, often with the connivance of the physician. It has been too easy for the unthinking doctor to meekly acquiese in the demand of the patient that he be admitted to the hospital for the purpose of getting roentgenography, or that the housewife be allowed to remain beyond the time when she could have been discharged, in order that she may get a desired further rest from household duties, to be paid for from insurance plans.

As I said before these are no problems of particular concern to our specialty. In fact, it is doubtful if many of us have given them any thought. Yet they are of concern to our hospitals and what concerns our hospitals should concern us. As a respected specialty in our institutions we could, by leadership and example, do much to correct these evils and improve the situation of our hospitals.

May I add one further observation not quite germane to my text, but one upon which I may be qualified to speak by some years of service on our National Examining Board. Unfortunately certain of our hospitals have seemed to imitate the closed-shop, by limiting all staff appointments to physicians certified by their Boards, on the assumption that this was an edict of the Boards. To the best of my knowledge this has never been the case. The Boards are vitally interested in maintaining the highest possible standards in all branches of medicine but have no desire and possess no power, to dictate appointments. Qualifications, not certification, should be the criteria. Senior appointments, whenever possible, should require certification; but to exclude younger men from all staff privileges until certified, would deprive them of opportunities that rightfully should be theirs. This is a matter which should be decided at the local level. Working under proper supervision, wherever indicated, would assure the hopital of the active services of these younger men and give them the added experience they should have.

In all that I have said I have endeavored to emphasize the advantages of team work, utilizing all indicated skills in allied professional fields. This implies the wide use of consultants in clinical practice and the sharing, or even delegation, of therapy, whenever the patient might benefit thereby. It implies close association with audiology, not only in research but in programs of conservation and rehabilitation, assuming those responsibilities that should be ours. It means, as a part of the medical profession, cooperating with our hospitals that they may continue to operate efficiently, providing the necessary quality of service.

A specialist has been defined as one who knows more about less. As such he is a valued and necessary member of the medical team. But it should be kept in mind that two heads are better than one, unless they both are on the same body.

The strength of specialism is knowing more about a limited field. Its weakness is that this knowledge is restricted to a limited field. If we recognize that limitation and utilize the available skills in other fields, we overcome our weaknesses and increase our strength.

In closing I wish to pay deserved tribute to the members of the Council who have served the Society so faithfully, and particularly to our efficient Secretary-Treasurer, Dr. Lindsay. We all know how much of the responsibility for the operations of the Society falls upon whoever holds this office.

Professional Bldg.

XXXIV

THE HARD OF HEARING INFANT

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Most of the statements and some sentences in this paper can be found in the references appended to it. They have been picked out because many years' experience, in a hospital for sick children in a clinic devoted to the prevention of deafness, have shown them to be true. Thy are emphasized here because some textbooks and papers continue to make other statements which are so incorrect and so harmful that they should be eliminated from medical teaching and belief.

The ignorance regarding the importance of hearing in a child under two years of age is appalling. Within the past year papers and speakers have endorsed half-truths or complete misstatements such as: "Deafness in a young child is usually obvious." But it isn't; it is often extremely hard to determine. "Arrangements should be made for training by the mother from the age of three and for special education from the age of five." The mother should start the training as soon as the defect is suspected—perhaps at 6 months of age—and the special education should be started, if possible, at the age of two, and certainly at the age of three. If these early critical years are lost the child's opportunity to acquire fluent speech is missed forever. "There is a paucity of research regarding intelligibility scores for very young hard of hearing children." But there has been a great amount of such work sincerely and excellently detailed. "Specific information relative to language development, speech and voice characteristics of these very young children does not appear in the literature at present." I would agree that it does not appear in the jargon of present literature which uses expressions such as "enrolled in an auditory training programme," "utilization of modern electronic equipment," "dynamic concepts of audiometry." It

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is however, to be found in the careful, reliable, simply written papers of investigators such as Gesell.

A clinic such as ours for the prevention of deafness in a hospital devoted to children has very many problems on its hands. These vary with the age of the child, with the age at which the loss of hearing appeared, with the causes of such hardness of hearing, with the hearing tests that must be used and with the various other defects and diseases of the little patients.

To such a clinic will come little children with gross abnormalities. Some will have defects of the hearing apparatus: middle ears discharging profusely, ear drums destroyed, congenital malformations of auricle, canal and middle ear. Some are deaf as the result of meningitis. Some will present severe behaviour problems: undue excitement, unduly disturbed, excessive shyness, violent temper tantrums, complete lack of co-operation. Some will have abnormalities of the central nervous system; cerebral agenesis, cerebral palsy, convulsions etc. We are asked how much hearing these children have, how much the hearing defect accounts for their behaviour, and what should be done for them. None of these will concern us here.

Fortunately there is another group which very much requires our help. What follows is a discussion of problems presented by a presumably healthy child below the age of two, normal in every respect except that the child does not seem to hear and cannot talk. Our goal with the deaf child is to make him as nearly a normal member of society as possible and so he must be taught to understand speech and to speak.

The first step is examination to exclude any organic aural defect. Then must follow an attempt to determine the hearing of the baby. The methods used vary with the age of the child and are described in a later section of this paper. The next step is to provide guidance for its parents and help for it if possible.

The majority of congenitally deaf children come to the clinic too late and go to preschool training class without any training in lip-reading and with voices that are dull, flat and lifeless. This occurs because two essentials in their training have been missed. It has not been started early enough. It has not been done by the potential teacher every baby has—its mother.

When the mother first suspects her child's deafness she will go to her pediatrician or to her general practitioner for the investigation of her fears. The time-honoured advice is that nothing can be done until the baby is older. That advice is wrong. At that moment the pediatrician has the opportunity to point out to her the necessity of the early training which is so vital for her child's future happiness. The pediatrician must convince the mother that she can teach the baby to lip-read. If there is any doubt that the baby has normal hearing, training should be started straight away.

Lip-reading by little babies is a very old story which has been greatly misbelieved. But in 1947 a doctor and his wife demonstrated that their congenitally completely deaf child of one year and ten weeks could respond by specific acts of behaviour to six different phrases which they spoke to the baby in a natural conversational manner.[7] This proof was demonstrated to a large audience and the knowledge was widely publicized. Since that time, in England, many babies have been benefited by this method and this early comprehension of speech has been followed by their beginning to try to vocalize spontaneously.

Most parents will be willing to give the necessary home training but first they need to be convinced by the confident assurance of the physician that benefit will come and that if they do not make the attempt for their baby they will be doing him an irreparable harm. If he is not given special training there is considerable risk that when he begins to walk freely he will become increasingly, almost even exclusively, preoccupied with exploration of the world of seeing.

The mother should not make the child lip-read[14]—it is better to encourage the child to lip-read by various devices. She should be told to talk to her baby naturally with her face in the light. She should speak every time the child looks at her when the situation is meaningful to the child. For example, when she picks up the baby's bottle, if she pauses for a moment, the child will look and the mother should say, "Here is your milk." Similarly with every situation the mother should encourage the child to expect words to accompany activities.

The parents should make a list of the words, phrases and sentences that they think they will want to use over and over again in many situations. Then they must make a point of using the list because it is repetition that is all-important.[9]

Here is a short list which many parents might find useful:—

BYE-BYE	NOT NOW	WAIT	UP	DOWN
ALL DONE	ALL GONE	NO MORE	MORE	NO

Here follows a longer list of words, phrases and sentences which would be used naturally in the given situations:

SUGGESTED LIP-READING FOR A VERY YOUNG DEAF CHILD.[13]

	6 MOS. TO 12 MOS.	12 MOS. TO 18 MOS.	18 MOS. TO 24 MOS.
BATH EXPERIENCE			
Nice bath	+		
You are going to have a *bath*—a nice bath		+	+
Splash the *water*	+		
Here's the *soap*		+	
Give mama the *soap* (holding out hand)	+		
Where's the *soap*		+	
Let's wash your *face*		+	
ears		+	
hands		+	
arms		+	
legs		+	
All done	+		
Here's the *towel*		+	
Wipe, or let's wipe your *face*			+
arms			+
Now we'll put on your *pyjamas*			+
or			
sleepers			+
or *nighty*			+
slippers			+

SUGGESTED LIP-READING—(Cont.)

	6 MOS. TO 12 MOS.	12 MOS. TO 18 MOS.	18 MOS. TO 24 MOS.
BED EXPERIENCE			
Bed time	+		
It's *bed* time now		+	
Let's go to *bed*		+	
Jump into *bed*			+
Here's your *bear,* rabbit, doll etc.			+
Lie *down*	+		
Kiss *mama, daddy*		+	
Bye-bye (waving)	+		
RISING EXPERIENCE			
It's time to get *up*		+	
Come on, *get up*		+	
Good *boy*	+		
Good *girl*	+		
Jump out		+	
Put on your *slippers*			+
bathrobe etc.			+
MEAL EXPERIENCE			
Here's your *breakfast*			+
Drink your *juice* (handing it to him)		+	
What a *good boy*	+		
Give mama (or daddy) the *cup*		+	
Here's your *pablum*		+	
Here's your *spoon*		+	
Eat your *pablum*		+	
Good boy	+		
Give mama the *bowl*		+	
Give mama the *spoon*		+	

SUGGESTED LIP-READING—(Cont.)

	6 MOS. TO 12 MOS.	12 MOS. TO 18 MOS.	18 MOS. TO 24 MOS.
MEAL EXPERIENCE—(cont.)			
Here's a nice *egg*			+
Eat up your *egg*			+
Let mama (or daddy) take off your *bib*			+
You're a good *boy*		+	
Now we'll get *down*			+
(Similarly with other meals)			
PLAY EXPERIENCES			
(a) *Kiddie car*		+	
Ride your *kiddie car*			+
Stop (holding up hand)	+		
Go (repeat *stop* and *go* while fun lasts)	+		
Let's get *off*		+	
Good boy	+		
Do you want to ride the *kiddie car* again?		+	
Get on, etc.		+	
(b) *Ball*	+		
Here's your *ball*		+	
Throw the *ball*		+	
Throw it *up*			+
Where is the *ball?*		+	
Get the *ball*			+
(c) *Doll*	+		
Hold your *doll*	+		
Put the *doll* to sleep		+	
Oh, poor *dolly* fell			+
Pick the *doll* up			+
Rock the *doll* (demonstrate)			+

SUGGESTED LIP-READING—(Cont.)

	6 MOS. TO 12 MOS.	12 MOS. TO 18 MOS.	18 MOS. TO 24 MOS.
PLAY EXPERIENCES—(cont.)			
Here's the doll's *mouth*			+
eyes			+
ears			+
arms			+
feet			+
Here's your *mouth*		+	
eyes, etc.		+	
Put the *doll* in the carriage			+
Wheel the *doll* (if the child can walk well)			+
(d) *Bear*	+		
Here's your *bear*	+		
Feel the bear (demonstrate)		+	
The *bear* is soft			+
Kiss your *bear*		+	
Where is the *bear's* mouth, nose, etc.			+
(e) *Water Play* in bath tub or a big dishpan, floating duck, fish, frog, etc.			
Here's the duck, Make the *duck* swim		+	
Here's the *fish*, etc.		+	
Give me the *duck*		+	
Good boy	+		
(f) *Participation in pie baking experience*			
Mama is going to make a *pie*			+
Here's the *rolling pin*			+
Here's some *dough* for you (Give child toy rolling pin)			+
Now you roll your *dough*			+
Put it in the pie *plate*			+
Now we'll put it in the *oven*			+
Shut the *oven*			+
(Later) My it *smells good* (sniffing with appreciation)			+
You smell		+	
It's *all done*		+	
Good boy	+		

Conversations like these, repeated again and again, will awaken a child's mind and establish communication and so security between parents and child. The parents should strive to get near the child. It is not enough to dress him, keep him clean, feed him. Where the parent has established communication the child is more or less reasonable. Lip-reading is one of the most important means of establishing this communication. Lip-reading is understanding what is said—it is not just speaking. Parents have difficulty understanding this.

The parents should also be told two things they should not do. Sign language must not be used. Words must not be used in an unnatural manner. A picture should be found—they are easily found —of an enthusiastic specially trained university graduate talking to a little child apparently endeavoring to get the baby to look at her lips and her tongue. This picture should be shown to the parents as an example of what they should not do when training their infants. A normal baby learns to hear and speak in a quite informal manner, and the hard of hearing baby will learn to understand its mother by casual and effortless watching of her face.

In all this the first aim of the doctor has been to make the parents help the child to hear by lip-reading. The second aim to which the attention of the parents must be directed is the preservation of the tone of the voice of the child.

The voice of a one year old deaf child is natural. It has rhythm and there are natural variations in loudness and in pitch. These variations are such as occur in the vocalization of children who can hear. Probably they are fewer in number.

The apparent normality of voice continues to about the age of 18 months: at that age a totally or very severely deaf child if left to himself usually loses interest in using his voice. He becomes more and more silent. Only when angry or afraid will he make a noise. The Ewings of Manchester state that in their experience if the deaf baby ceases to use his voice its natural quality can never be recovered.[2, 8] From then on his voice deteriorates rapidly until at the age of three his voice is flat and ugly. The point is that the voice no longer develops—instead it deteriorates.

The way to prevent this deterioration—the way to develop the baby's speech—is to preserve his interest in his own vocal character-

istics even though he cannot hear any sound, and to encourage him constantly to use his voice to attract attention to his wants. Gradually he should be made to understand the kind of voice that pleases others.

The parent[14] should respond to all pleasant vocalization and refuse to respond to unpleasant or harsh sounds. The child will be anxious to get a response and will use a pleasant voice to do so.

The parents must be made to understand this thoroughly. It then becomes their duty to encourage the child to keep his voice and use it. If this is done the child of three, entering the preschool hard-of-hearing class will have a voice which will be far superior to that of the untrained deaf child. The earlier this training is begun and the more strenuously it is kept up the better for the small child.

Although the mother will do most of the training she will need help and encouragement.[9] It should be possible for her to come to the clinic and explain her difficulties to someone who is both a qualified teacher of the deaf and a specialist at work with young deaf children. Such help becomes more and more necessary as the child approaches the age of three when he should be able to be entered in a preschool hard-of-hearing class. Because at that age the child should have reached a stage of "speech readiness."[7] As soon as he has reached that state he should get regular daily lessons from a skilled, qualified teacher. The development of intelligible speech by a deaf child is the desired goal but it is only achieved by long patient training by a devoted teacher of the deaf.

TESTS OF HEARING

I will now describe some of the methods to determine the hearing of a baby.

The Newborn Infant: Congenital deafness is not detected, as a rule, until the latter part of the first year of life. This is because the average mother of a normal appearing baby never suspects that her baby could be deaf. But when a normal baby is a candidate for adoption or when an abnormal baby is being examined for the cause of its abnormality its ability to hear becomes an important matter for investigation.

Forty-six newborn infants between thirty minutes and eight days of age were recently investigated by Richmond, Grossman and

Lustman[12] and they recommend that their procedure be made standard in all nurseries as part of the routine of neonatal evaluation.

Their technique for testing these infants is performed with a cowbell with an intensity of 113 decibels with two dominant overtones of 2650 and 8000 cycles per second held about 33 cm from the infant's head. When the bell is struck the baby may blink its eyes, or tighten the closed lids, or suddenly move its trunk or extremities.

The newborn infant should be tested only when reasonably quiet; never while in deep sleep, actively nursing, or crying. Light sleep is the best condition for a hearing test.

If the newborn does not respond to this procedure it should be re-tested every month until a decision regarding its hearing can be made.

It is one thing to state that the baby can hear, it is a much harder thing to be certain that it cannot. In some babies the determination can be made as early as eight weeks of age, but there are many babies who cannot be so determined by the twelfth month and a few not till they are over two years of age.

The behaviour of a baby changes as it grows older and in consequence the tests must be modified accordingly.

An attempt will therefore be made to state how a baby can be expected to respond to a sound at four ages: six months, twelve months, eighteen months and twenty-four months.

The tests require three people. The mother or a nurse should hold or attend the child. The second should offer the stimuli and record the results. The third should concentrate on observing the child's behaviour and response. No tests are fool-proof.[5] Any test may be misleading in either direction because of varying degrees of attention. Also, any child may develop a complete disregard of a sound it does not want to hear or which has no meaning for it. No matter what test is being used acute observation of the baby's behaviour is the great essential.

The tests should be made from a distance of about six feet and without the child watching.[3] It should be impossible for the child to be aware of the presence of the persons making the sounds. The observers should give no sign that such sounds are present.

These tests are eminently practical and are all so simple that they can be done at home. They are qualitative and not quantitative. They will only determine whether a sound is or is not heard. They will not measure or even detect slight defects. They must be repeated several times to insure reasonable accuracy.

At six months: Up to six months a baby's response to sound may be reflex or learned.

A normally hearing infant until it is three months of age responds to loud sounds by a reflex such as by blinking, by a jerking of the body or head or by a change in facial expression. A bell or drum or tapping a cup with a spoon can be used to produce the reaction.

After this age the reflex tends to disappear but in the severely deafened child it may persist till nearly the twelfth month. This is because the babies with impaired acuity have heard fewer sounds and had fewer opportunities of connecting such sounds as they could hear with their meaning.

Some babies will respond reflexly for a time and then the response may change to a smile or an expression of dislike showing that the stimulus holds a meaning for him.

Others after responding two or more times will appear to ignore the sound.

Sudden unusual loud noises such as clapping the hands, turning on the radio, an auto backfiring, an aeroplane overhead, dogs barking, should produce the above responses. If they do not the baby is probably severely deaf.

At twelve months: The same stimuli can be used but the quiet voice should be more important to the child than a loud noise. The closer the child is to twelve months of age the more it should be able not merely to hear a sound, but after several attempts, to accurately locate its source. If it does not respond to the sound of a voice it is almost certain that he is deaf, mentally deficient or has some other form of gross defect.

Most children at this age can discriminate between certain sounds which hold meaning for the child.

It is because a child is partially deaf that the process is delayed by which sounds normally would become meaningful to him.

Its voice will be indistinguishable from that of a normal hearing child.

At eighteen months: At this age the normal child tends to ignore loud percussion sounds and loud noises. It becomes necessary to win the child's interest, attention, willingness to co-operate, and this will be more effectively achieved by using quiet speech than by loud voice. Meaningful sounds should not be neglected. The mother can usually tell you of sounds which might have a meaning for the child. The examiner should use these.

The observer should stay with the child and observe it intently. The mother, while remaining out of sight, should speak to the child from shorter and shorter distances and may speak more and more loudly until a response is observed or until the observer is satisfied that the child has not heard.[5]

The voice of the severely deaf child will be becoming strained, flat and ugly.

The normal child should walk at eighteen months. If the labyrinth is also involved the severely deaf child may walk clumsily or shuffle its feet.

At twenty-four months: Children at this age have a capacity to ignore completely a certain amount of noise. Before tests are made the child should be observed carefully to determine the things it is presently interested in and accurately to estimate its mental ability, personality and emotional attitude. Correct estimation of these things may lead the examiner to choose sound stimuli which may provoke response from the child.

A caloric test should be performed on every extremely deaf child.

The test should be described to the mother and she should be assured that no harm will be caused the child. The mother should be present and may assist.

The infant can, if deemed advisable, be tested at its first visit. An older child should not be tested until, as the result of several visits, it has confidence and trust in the doctors and nurses.

The test should be performed to produce horizontal nystagmus. Many children who have had meningitis may have no ocular response,

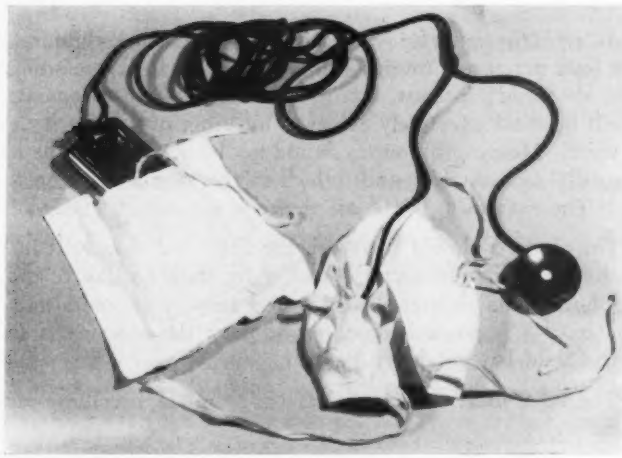

Fig. 1.

however, some of these may have some residual hearing.[9] Absence of the ocular response often has occurred in children with no demonstrable hearing.

It is our policy to teach a severely hard of hearing child to use a hearing aid at the earliest age it will tolerate the aid.

In one clinic in England an attempt is being made to make babies aware of sound by using hearing aids.[7]

We have been using a powerful Zenith hearing aid attached by a long heavy cord to two flat earphones (Fig. 1). The latter are tied in pockets on a washable cotton hood make to fit the baby.

The normal baby can hear his own voice. The fact that other people's voices and his own are alive to him, gives him a powerful incentive to learn to use his own voice. To the profoundly deaf baby, his mother's and his own voice are dead and he is without incentive to learn to use his voice.

The rate at which speech develops, is, of course, most variable.[10] The average normal hearing child according to Gesell, will say a simple repeated syllable at eight months of age: it will say three words at fourteen months of age and it may have 200 words at twenty-four months of age. It takes nearly two years of intensive listening before it puts together a few combinations of words. Its ability to imitate sounds is greatest in its first three years of life. Hearing, thought and mental development are closely linked. The normal hearing baby is influenced in his personal relationships with other people by the sound of their voices when they play with him or talk with him. The deaf baby—because he cannot hear—will steadily develop a lag between his observed ability and his innate ability.[4]

"To hear speech imperfectly is far better for children than not to hear it at all. To hear the various sounds incidental to its daily life and to be able to associate them with visual experience lessens appreciably the handicap of deafness." So we have been trying this hearing aid to find out if we can make sounds come alive to profoundly deafened babies. It will take a long time to determine the best technique to follow and a still longer time to get enough severely deafened infants to make statements regarding its value.

The present set of instructions sent to the ward with the machine is as follows:

INSTRUCTIONS FOR NURSE ATTENDING DEAF INFANT

Hearing Aid. Take great care that no damage is done to any part of the apparatus.

Do not turn wheel higher than the intensity you are instructed to use. If this intensity seems to annoy the child—report it to the house surgeon.

Always turn wheel to zero when not in use.

Behavior With Child. Do your best to establish communication between yourself and the child. The more you achieve this, the more secure the child will feel and the better it will behave.

Words To Be Used. Do your best to use the following words nearly exclusively. When you are speaking them try to have your own face in the light. We hope that gradually the baby will learn

to watch your face when you are speaking to it and gradually learn to know what you are saying.

No	Down	More
Up	All Gone	Bye-Bye

Repetition of words and simple phrases is most important.[9]

Time and experience will undoubtedly lead to changes.

CONCLUSIONS

In closing I want to emphasize again—that ignorance regarding the importance of hearing in infants is widespread—that the literature and texts are full of half-truths and complete mistatements regarding it.

These misstatements must be rooted out. In their place we must establish the following facts which every doctor should know and every graduating student should be taught.

Investigation in schools for the deaf in England and the United States during the past 24 years have shown that a majority of the pupils became deaf before the age of two and also that few are totally deaf.[7] As a rule there is some residual hearing which should be made use of in the education of the child.

It is, therefore, of the utmost importance to detect deafness and commence training as early in life as possible.[3]

Deafness can be detected in the first year of life.[9] During this time, fantastic and elaborate tests of hearing are unnecessary.

The infant can learn to comprehend speech through lip-reading by casual and effortless watching of its mother's face.

Many deaf infants have achieved articulation readily and also some speech without loss of spontaneity.[7]

The methods and nature of the examination and training must be adapted to the stage of the child's mental growth.

We must convince the pediatricians and parents that little deaf children can be taught both to understand speech, and to preserve the tone of their voices.

170 St. George St.

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XXXV

THE DEVELOPMENT AND ADULT STRUCTURE OF THE MALLEUS, INCUS AND STAPES

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A series of journal articles, emanating from the Anatomical Laboratories of the University of Wisconsin and of Northwestern University Medical School, have reported the results of an inclusive otological study of the developmental and adult anatomy of the auditory and of the otic capsule.

The early reports dealt chiefly with the following subjects: the development of the stapes;[1, 4] the developmental and normal adult structure of the fissula ante fenestram;[5] the aberrant form and pathological contents of the fissula;[6] the development of the otic capsule and of the extracapsular tissues.[4, 7, 8] Later, the original program was extended to include those special portions of the capsule in which late histological alteration regularly occurs; these are the cochlear aqueduct and periotic duct,[9] the tympanic wall of the lateral semicircular canal (the region of surgical fenestration),[2] the cranial (external) aperture of the vestibular aqueduct[3, 11, 14] and the cochlear fenestra (round window).[12]

From the Department of Anatomy of the University of Wisconsin and the Department of Anatomy of Northwestern University Medical School (Contribution No. 606 from the latter). This study was conducted with the aid of grants provided by the Central Bureau of Research of the American Otological Society and by the Wisconsin Alumni Research Foundation.

Paper read at the Sixty-seventh Annual Meeting of the American Association of Anatomists, University of Texas, Medical Branch, Galveston, Texas, April 7 to 9, 1954.

The present report will account for the development of the malleus and its anterior process, for the morphogenesis of Meckel's cartilage and the incus. The development of the stapes and the otic capsule will be reviewed.[10, 13]

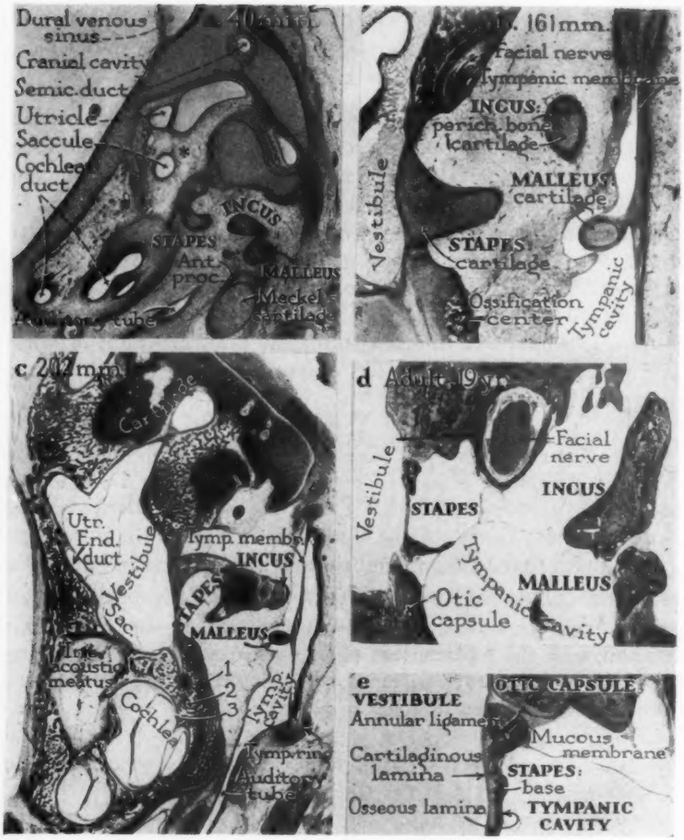
MATERIALS AND METHODS

The study of the auditory ossicles is based upon an examination of some 200 series of sections. From the extensive sets of microscopic sections in the otological collection at the University of Wisconsin, crucial stages were selected for description herein. Reconstructions were prepared from the following fetal stages (Figures 8 to 10): 40 mm, 62 mm, 84 mm, 100 mm, 120 mm, 126 mm, 161 mm, 190 mm, and 222 mm. The following stages were photomicrographed: fetuses of 40 mm, 100 mm, 117 mm, 120 mm, 126 mm, 161 mm, 183 mm, 190 mm, 222 mm, 243 mm, 280 mm, 290 mm; infants (6 and 7 months of age); child (13 years of age); adults (19, 40 and 62 years of age).

The illustrations which were prepared from photomicrographs are arranged in such a way that each set deals with a single major aspect of the discussion: Figures 1 to 3 are concerned with the general development course of the three ossicles and of the otic capsule; Figure 4, with that of the manubrium of the malleus and of the long crus of the incus; Figure 5, with the postnatal remodelling of the long crus; Figure 6, with the development of the short crus of the incus and with the replacement of Meckel's cartilage by ligamentous tissue. Figure 11 serves to summarize pictorially the chief features in ossicular development.

OBSERVATIONS AND DISCUSSION

A. *Early cartilaginous development of the ossicles. 28-mm embryo.* At this stage the malleus, incus, and Meckel's cartilage are composed of young cartilage cells. The stapes and the otic capsule are undergoing a change from precartilage to true cartilage. The short crus of the incus is in contact with the lateral wall of the otic capsule. Both malleus and incus are independent at the site of their articulation. The future incudostapedial joint is similarly recognizable. The incus and stapes are independent of the branchial skeleton, but the malleus is still broadly continuous with Meckel's cartilage.[10]



Dural venous sinus
Cranial cavity
Semic. duct
Utricle
Saccule
Cochlear duct
INCUS
STAPES
Ant. proc.
MALLEUS
Meckel cartilage
161 mm.
Facial nerve
Tympanic membrane
INCUS:
perich. bone
cartilage
Vestibule
MALLEUS:
cartilage
STAPES:
cartilage
Ossification center
Tympanic cavity
c
Cartilage
Utr.
End. duct
Vestibule
Sac.
Tymp. membr.
INCUS
STAPES
MALLEUS
acoustic meatus
Cochlea
1
2
3
Tymp. cavity
Tymp. ring
Auditory tube
d
Facial nerve
Vestibule
INCUS
STAPES
Tympanic cavity
MALLEUS
Otic capsule
e
VESTIBULE
OTIC CAPSULE
Annular ligament
Mucous membrane
Cartilaginous lamina
STAPES:
base
Osseous lamina
TYMPANIC CAVITY

Figs. 1*a* to 1*d*.—Photomicrographs of transverse sections selected to demonstrate the general features in the development of the otic capsule and auditory ossicles, in four specimens. Fig. 1*a* and 1*b*, X 11; Fig. 1*c*, X 5; Fig. 1*d*, X 6; Fig. 1*e*, X 16. Fig. 1*a*, fetus of 40 mm (9 weeks), Wisconsin series 168 (slide 8, line 3, section 2); Fig. 1*b*, fetus of 161 mm (19 wks.), ser. 13 (sl. 42, line 2, sect. 2); Fig. 1*c*, fetus of 202 mm (23 wks.), ser. 70 (sl. 27, line 2, sect. 3); Figs. 1*d* and 1*e*, adult of 19 years, ser. P29 (sections 328 and 323, respectively).

Abbreviations in these and in succeeding figures are shortened forms of the full words: for example, *Ant. proc.*, for anterior process; *Int.*, for internal; *Perich.*, for perichondral; *Sac.*, for saccule; *Semic.*, for semicircular.

Fig. 1*a*.—In the fetus of 9 weeks (40 mm), the otic capsule and the auditory ossicles, although definitively formed, are still cartilaginous. The stapes, still annular rather than stapedial, is lodged medially in tissue which now closes the area of the future vestibular fenestra. A diverticulum of the pharyngeal epithelium, advancing toward the ossicles, is the primordium of the tympanic cavity. The future vestibule (indicated by asterisk) is still a group of coalescing vacuoles in embryonic periotic tissue.

Fig. 1*b*.—In the fetus of approximately 19 weeks (161 mm), continuing increase in size of all constituents of auditory apparatus has been accompanied by the early stage in bone-formation (seen first in the fetus of 16 weeks, Fig. 8*e*). The long crus of the incus has acquired an investment of perichondral bone, and a similar layer is about to form in the stapes. Ossification has not yet spread from the solitary center in the body and neck of the malleus to the manubrium (compare reconstruction, Fig. 9*a*).

Fig. 1*c*.—In the fetus of 23 weeks (202 mm) the persistence of cartilage in the manubrium of the malleus, in the lenticular process of the incus and in the basal and capital extremities of the stapes is matched by its presence in the canalicular division of the otic capsule. The crura of the stapes are formed in perichondral bone. The three typical osseous laminae are now present in the capsule: periosteal (at 1), intrachondrial (at 2) and endosteal (at 3).

Fig. 1*d*.—In their adult form the malleus and incus possess an almost solid structure. The stapes, on the contrary, has become excessively thin through late fetal destruction of periosteal bone on its obturator wall. Its base is two-layered (as shown at increased magnification in the following figure, for an area corresponding to that partly blocked out in this section).

Fig. 1*e*.—The base of the adult stapes is bilaminar; the osseous lamina forms the tympanic aspect, whereas cartilage is situated on the vestibular side. Canals for the transmission of blood-vessels, even though situated near the chondral lamina, are invariably lined by an osseous shell.

Although all of these structures are in an early stage of cartilaginous development, there are already two prominent structures, formed in membrane bone, located near Meckel's cartilage. One of these is the osseous mandible, situated along the anterior surface of the distal part of Meckel's cartilage. The other is the primordium of the anterior process (*processus gracilis*) of the malleus, which appears as an independent rod of membrane bone; situated at the free surface of the perichondrium on the medial aspect of Meckel's cartilage, it is entirely separate from the latter and from the malleus (compare 40-mm specimen, Fig. 1*a*).

40-*mm fetus.* In the 9-week fetus, the stapes has enlarged and its base is flattened in the vestibular (oval) window (Fig. 1*a*). Actually, the basal portion is continuous with the vestibular window; the two are separately distinguishable because of a concentration of mesenchymal cells, which serves to mark the site of the future annular ligament (Fig. 1*a*).

The malleus and incus have undergone comparable increase in size. The anterior process, even now a distinct rod of membrane bone, is separate from the malleus (Fig. 8*a*); in being segregated and already osseous, it belongs in a category with the tympanic ring. The lateral process (out of view in Fig. 8*a*) has appeared for the first time.

The ossicles now are cartilaginous and their zones of future articulation are identifiable (Fig. 8*a*). Each of the ear-bones begins to assume the form which is characteristic of the adult: in the stapes a flattened basal part is prominent; the crura of the incus are well developed; the head and manubrium of the malleus are likewise distinct (Fig. 8*a*).

Just prior to this stage (in the fetus of 36 mm, or 9 weeks), the tympanic "ring" makes its initial appearance as an incomplete annulet formed in membrane bone. All portions of the otic (endolymphatic) labyrinth are formed, and in the region of the future vestibule (Fig. 1*a*, at *) the occurrence of vacuolated spaces predicts the production of a continuous system of periotic (perilymphatic) labyrinthic spaces.

62-*mm fetus.* Within the two-week period between the 40-mm and 62-mm stages, the ossicles have almost doubled in size (Fig. 8*b*; compare Fig. 8*a*). Additionally, the morphological features which

are basic to the naming of the ossicles are more prominently developed: in becoming further flattened medially, the stapes appears stirrup-like; the body and short crus of the "anvil" are more definitely formed, as are the head and manubrium of the "hammer."

In this specimen the osseous anterior process is relatively small and distally placed in relation to the malleus (Fig. 8*b*). In other specimens it may be closer to the malleus (Figs. 8*a* and 8*d*), but further from Meckel's cartilage (Fig. 8*d*).

84-*mm fetus.* Within a week's time, between the 62-mm (11-week) and 84-mm (12-week) stages, the ossicles have increased their over-all dimensions by approximately one and one-half times (Fig. 8*c*; compare Fig. 8*b*). Yet, in none of the three has the process of ossification been initiated; nor has ossification begun in the otic capsule. Meckel's cartilage is still broadly continuous with the head of the ossicle (Fig. 8*c*). As seen histologically, the base of the stapes rests in precartilaginous tissue which closes the vestibular window; the latter is related medially to a thin stratum of periotic tissue of the newly-formed vestibule.

100-*mm fetus.* The ossicles at this stage, although still in chondrified form, forecast their true adult morphology. The base of the stapes is lipped circumferentially in accommodation to the form of the vestibular window; the head is foveate for reception of the long crus of the incus; the crura are markedly bowed. The stapes and incus are lodged in mesenchymal tissue; mucous membrane has reached the manubrium of the malleus.

Meckel's cartilage has attained maximum dimensions (Fig. 8*d*). The articulating surfaces are more definite and have increased in size in the location of the future joint cavities.

The anterior process of the malleus, formed in membrane bone, is adjacent to the neck of the malleus itself, but not yet joined to the latter (Fig. 6*a*).

B. *Osteogenesis and later development.* 117-*mm fetus.* At this stage an initial step has been taken in the ossification of the incus: the ossicle has now acquired a thin perichondral shell on the anterior aspect of the long crus (Fig. 4*d*). Calcification of the cartilaginous matrix is under way internal to this investment of bone. Through

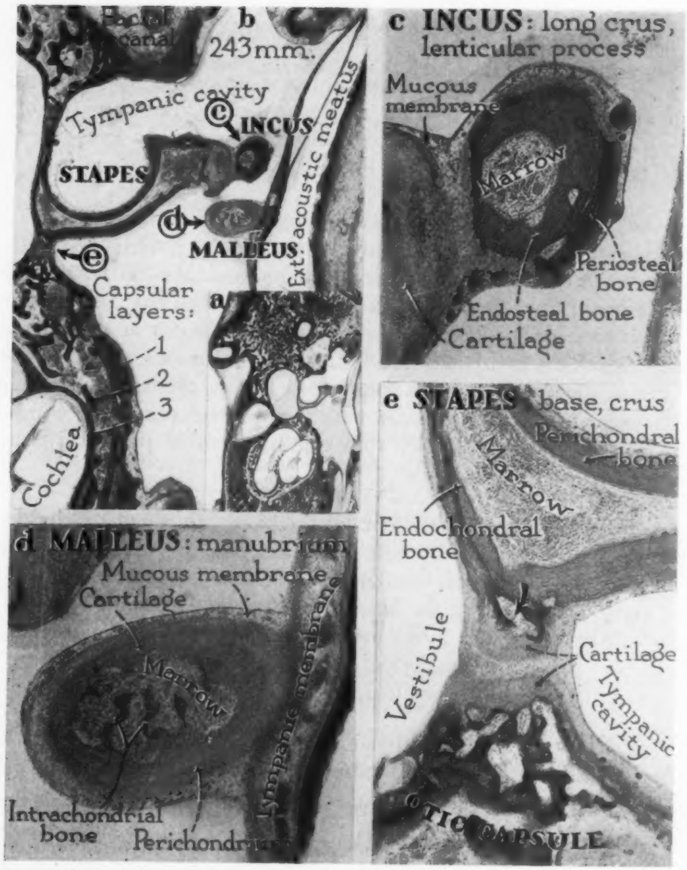

b
243mm.
Tympanic cavity
INCUS
STAPES
MALLEUS
Ext. acoustic meatus
Capsular layers:
1
2
3
Cochlea
a
c INCUS: long crus, lenticular process
Mucous membrane
Marrow
Periosteal bone
Endosteal bone
Cartilage
d MALLEUS: manubrium
Mucous membrane
Cartilage
Marrow
Tympanic membrane
Intrachondrial bone
Perichondrium
e STAPES: base, crus
Perichondral bone
Marrow
Endochondral bone
Vestibule
Cartilage
Tympanic cavity
OTIC CAPSULE

Fig. 2*a* to 2*e*.—Photomicrographs of a transverse section; the development of the otic capsule and auditory ossicles continued; fetus of 243 mm (27 wks.). Fig. 2*a*, X 2; Fig. 2*b*, X 10; Figs. 2*c* to 2*e*, X 50. Ser. 89 (sl. 23, line 1, sect. 2).

Fig. 2*a*.—The fetal otic capsule and ossicles, in their topographical relationships. Details of structure are shown in the accompanying illustrations.

Fig. 2*b*.—The ossicles and related tympanic, otic (endolymphatic) and periotic (perilymphatic) spaces; demonstrating especially the form and structure of the auditory ossicles, a selected area of each of which (at encircled letter) is shown at higher magnification in the succeeding figures (Figs. 2*c to* 2*e*).

Fig. 2*c*.—In the long crus of the incus, endosteal bone encloses a marrow cavity of diminishing size. The lenticular process is cartilaginous, and will remain so throughout life.

Fig. 2*d*.—In the manubrium of the malleus, cartilage, persisting externally, covers intrachondrial bone. Perichondral bone is absent.

Fig. 2*e*.—On the obturator aspect of the stapedial base and crus, perichondral bone is still present; on the vestibular aspect of the base, the cartilage remains intact. The arrow points to a vascular canal. Concurrently with removal of the perichondral layer which forms the obturator wall, endochondral bone will cover the opposite (tympanic) aspect of the base (see Fig. 3*e*) and the facing surface of the stapedial head.

the spread of the perichondral layer from this solitary center and as a result, too, of the production of endochondral bone, the entire incus, with the exception of the articular area and the apex of the short crus, will ultimately be ossified (see Figs. 4*e* to 4*h*). The short crus of the incus is still cartilaginous and is in contact with the otic capsule at its lateral extremity. However, the two cartilaginous masses are separated by a condensation of mesenchymal cells.

These steps in morphogenesis of the incus are matched, somewhat later, by the progressive development of the malleus (except for the manubrium), but not by those which bring the stapes to maturity.

120-*mm fetus.* In this 16-week specimen, ossification has begun in the neck of the malleus (Figs. 8*e* and 6*b*). Here, as in the case of the incus of the younger fetus (117 mm), a thin, periosteal bony shell precedes endochondral changes and calcification of the cartilage matrix. The anterior process of the malleus remains separate from the neck of the ossicle (Fig. 8*e*).

Meckel's cartilage is still broadly continuous with the malleus, to which branchial bar it owes its origin. The cartilage never ossifies. However, as might be expected in the reclamation of any part of a branchial skeleton for new uses, Meckel's cartilage makes a contribution to the auditory apparatus of the adult; it does so by, first, undergoing disorganization, then, second, conversion of the altered chondral tissue into ligament. In the present stage, deorganization is evidenced in the zone of junction of Meckel's cartilage with the malleus: the cells peripherally placed are beginning to lose their identity and, thus, to revert to a fibroblastic state (compare 161-mm stage, Fig. 7*a*).

The incus possesses a perichondral collar which advances from its center of ossification along the long crus and ascends to the anterior portion of the body (Fig. 8*e*).

126-*mm fetus.* At this stage (approximately 16½ weeks) a perichondral ring of bone is prominent at the ossification center in the incus. The underlying calcifying cartilage is being invaded by osteogenic tissue at the anterior aspect of the body and at the medial, lateral and posterior surfaces of the long crus (Figs. 8*f* and 4*e*). Whereas, in the 117-mm stage (Fig. 4*d*), perichondral bone appeared as a mere pellicle on one surface of the long crus, in the 126-mm fetus

the outer layer of bone forms an almost complete investment of appreciable thickness—complete, in fact, except where continuity is retained between portions of osteogenic tissue situated external and internal to the perichondral layer (Fig. 4*e*). The cartilage which exhibited calcification in the preceding stage is now being eroded by the vascular osteogenic buds. Yet, some of the cartilage, farther removed from the site of invasion, retains its primitive, unaltered, structure.

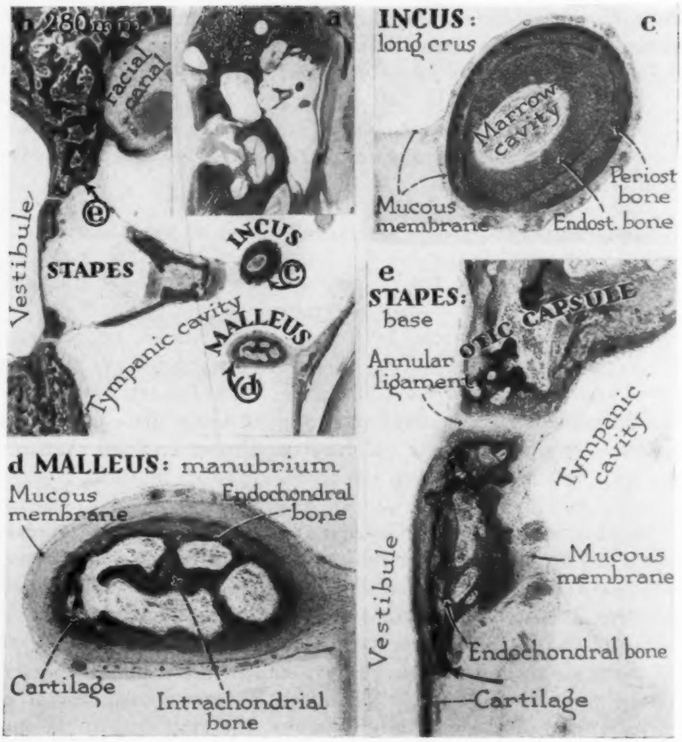
Simultaneously a similar change is occurring in the neck of the malleus; however, the manubrium of the latter ossicle remains cartilaginous (Fig. 4*a*).

In the stapes there is as yet no indication of bone formation.

161-*mm fetus.* In several respects this 19-week specimen represents a crucial stage in ossicular morphogenesis (Fig. 9*a*): perichondral bone now encircles both crura of the stapes; endochondral bone is spreading in the malleus and incus toward the boundaries of the previously formed perichondral shell; Meckel's cartilage is undergoing deorganization; the anterior process of the malleus has attained maximum length; the three ossicles have almost attained maximum size.

In the progress of ossification, perichondral bone has spread cranialward on the body of the incus, and caudalward on the long crus; in the malleus, bone has reached the summit of the head, is descending to the manubrium and spreading anteriorly to the area of continuity of the malleus with Meckel's cartilage (Figs. 6*c* and 9*a*). Beneath the perichondral layer, endochondral bone is now developing rapidly (Fig. 9*a*). Therefore, as seen in sections at the transverse level of the vestibular window, the long crus of the incus is acquiring endochondral bone internal to the investing layer of perichondral bone (Fig. 1*b*), while the manubrium of the malleus remains cartilaginous. The short crus of the incus is likewise composed wholly of unaltered cartilage (Fig. 9*a*).

In the stapes, perichondral bone has spread from the single center on the obturator aspect of the base, but not far enough to form an uninterrupted "ring" of bone (that is, to be continuous across the base, along the crura and across the head of the ossicle). When such continuity is established (in the 183-mm fetus), growth of the stapes will cease.


280 mm.
a
Facial canal
Vestibule
e
STAPES
INCUS
c
Tympanic cavity
MALLEUS
d
INCUS: long crus
c
Marrow cavity
Periost bone
Mucous membrane
Endost. bone
e
STAPES: base
OTIC CAPSULE
Annular ligament
Tympanic cavity
Vestibule
Mucous membrane
Endochondral bone
Cartilage
d MALLEUS: manubrium
Mucous membrane
Endochondral bone
Cartilage
Intrachondrial bone

Figs. 3*a* to 3*e*.—Photomicrographs of a transverse section; development of the otic capsule and the auditory ossicles, concluded; fetus of 280 mm (31 wks.). Fig. 3*a*, X 2; Fig. 3*b*, X 10; Figs. 3*c* to 3*e*, X 50. Figs. 3*a* to 3*e*, ser. 116A (sl. 38, line 2, sect. 2).

Figs. 3*a* and 3*b*.—The ossicles and their relation to the otic capsule and to the tympanic mucous membrane. In Fig. 3*b* the structures shown at increased magnifications in the three succeeding figures are indicated by encircled arrows.

Fig. 3*c*.—In the distal end of the long crus of the incus, a considerable layer of endosteal bone is invested by a periosteal stratum.

Fig. 3*d*.—Unlike the long crus of the incus, the distal portion of the manubrium possesses no periosteal bone; instead, cartilage forms the outer layer. Intrachondrial bone is present internally in a relatively large marrow cavity.

Fig. 3*e*.—A layer of endosteal bone spreads along the tympanic (external) surface of the cartilage of the base of the stapes, converting it into the bilaminar form which typifies the adult architecture of the stapedial footplate. The tip of the advancing osseous layer is indicated by an arrow.

Again employing the long crus of the incus for convenient demonstration of typical ossicular ossification, it is to be noted that intrachondrial bone has now been produced through rapid change in the cartilage (Fig. 4*f*) which, in an earlier stage (Fig. 4*e*) was just being invaded by ostengenic tissue. In still more advanced stages, endochondral bone will outbulk this "mixed" tissue, completely filling the now capacious marrow cavity (compare 290-mm stage, Fig. 4*h*).

The anterior process of the malleus, long since fully formed in bone, is now fused with the neck of the ossicle (Fig. 9*a*).

At the malleolar extremity of Meckel's cartilage (where the latter branchial bar was broadly continuous with the ossicle), two changes are concurrently under way: formation of endochondral bone is just being initiated; deorganization of Meckel's cartilage is in progress, preparatory to conversion of the tissue into that of the anterior ligament of the malleus (Fig. 7*a*). The effect of this latter change is evident "grossly" when the ossicles are shown in a reconstruction (Fig. 9*a*). Within a five-week period, the cartilage of the originally broad branchial bar will be reduced to a mere remnant lodged in the ligament (Figs. 10*c* and 10*d*). Shortly thereafter the cartilage will disappear completely.

Ossification is well advanced in the otic capsule as a whole (Fig. 1*b*). However, while on the posterior aspect of the vestibular window the typical layers of bone are present (periosteal, intrachondrial and endosteal), cartilaginous tissue persists in considerable amount on the anterior aspect of the fenestra; here the chondral tissue is broadly continuous with that which surrounds the fissula ante fenestram.

183-*mm fetus.* At this stage in the development of otological structures, the otic capsule and the auditory ossicles have almost attained adult dimensions. However, in the further course of morphogenesis, the otic capsule will become imbedded in periosteal bone; internally it will acquire a petrous character and will undergo regional remodelling (on the tympanic wall, at the cochlear fenestra, along the course of the fissula ante fenestram and at the cranial orifice of the vestibular aqueduct); the malleus and the incus will become quite solid; the stapes will lose at least half of its bulk. These changes have been fully described and amply figured in earlier reports by the authors and their colleagues.[1, 4]

In the midportion of the long crus of the incus, the formation of endochondral bone is now well under way internal to the shell of perichondral bone, and is being applied to the latter (Fig. 4*g*); however, some cartilage persists, and islets of intrachondrial bone are still to be found scattered sparsely through the marrow cavity. It will be recalled that in a specimen five weeks younger (that is, in one of 16½ weeks, or 126 mm), perichondral bone was just appearing (Fig. 4*e*). Through the contiuing production of endochondral bone, the marrow cavity will be virtually obliterated in the fetus of 32 weeks (or 290 mm, Fig. 4*b*), completely so in the term fetus, in the newborn and in early postnatal specimens (Fig. 5*a*).

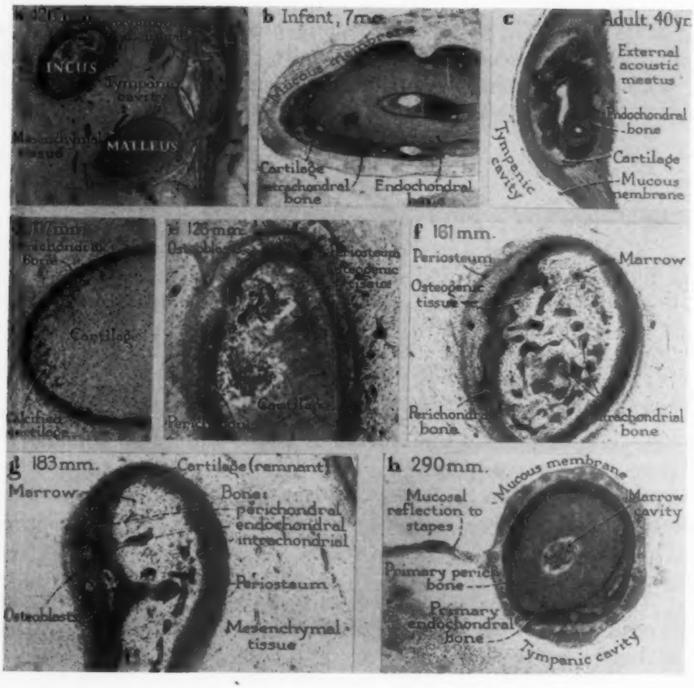
190-*mm fetus.* In the malleus and incus of this 22-week specimen, endochondral bone, in the course of progressive spread, has almost everywhere reached the limits of the perichondral layer (Fig. 9*b*). Cartilage remains in the three ossicles at the sites of true articulation (incudomalleolar and incudostapedial) and in areas of attachment of ligaments or membranes, namely, in the manubrium of the malleus, in the short crus of the incus and on the base of the stapes, but not at the attachment of the future anterior ligament.

The malleus is now ossified in the portion immediately related to the anterior process, and fusion of these contiguous surfaces has already taken place (Fig. 6*d*). Within this part of the malleus, endochondral bone is replacing cartilage in a series of steps comparable to those observed in the long crus of the incus in a younger specimen (see Fig. 4*e*, 126-mm fetus).

The manubrium, while destined to undergo further ossification, will never become osseous at its distal end; cartilage will remain there as a thin collar.

202-*mm fetus.* In the 23-week specimen, just a week after the stage just described, the cartilage of the neck of the stapes is being eroded; mere remnants of endochondral bone remain in the crura. The crura are formed of perichondral bone (Fig. 1*c*).

The articular extremity of the long crus of the incus lags in development; the articular surface is cartilaginous (as is the related part of the stapedial head). Development in the long crus is advanced beyond the stage represented by the lenticular process—since it already possesses an appreciable layer of endochondral bone.


INCUS
MALLEUS
b Infant, 7mo.
Mucous membrane
Cartilage
intrachondral bone
Endochondral bone
c
Adult, 40yr.
External acoustic meatus
Endochondral bone
Cartilage
Mucous membrane
Tympanic cavity
Cartilage
f 161 mm.
Periosteum
Marrow
Osteogenic tissue
Perichondral bone
bone
g 183 mm.
Cartilage (remnant)
Marrow
Bone: perichondral endochondral intrachondrial
Periosteum
Osteoblasts
Mesenchymal tissue
h 290 mm.
Mucous membrane
Mucosal reflection to stapes
Marrow cavity
Primary perich. bone
Primary endochondral bone
Tympanic cavity

Figs. 4*a* to 4*h*.—Photomicrographs of transverse sections through the manubrium of the malleus (Figs. 4*a* to 4*c*) and through the long crus of the incus (Figs. 4*d* to 4*h*). Fig. 4*a*, X 24; Fig. 4*b*, X 28; Fig. 4*c*, X 33; Figs. 4*d*, 4*f* and 4*g*, X 38; Fig. 4*e*, X 57; Fig. 4*h*, X 30. Fig. 4*a*, fetus of 126 mm (16 wks.), ser. 11 (sl. 30, line 2, sect. 4); Fig. 4*b*, infant of 7 months, ser. B120 (sl. 21, line 2, sect. 2); Fig. 4*c*, adult of 40 years, ser. P43 (sect. 500); Fig. 4*d*, fetus of 117 mm (16 wks.) ser. 55 (sl. 20, sect. 9); Fig. 4*e*, fetus of 126 mm (16 wks.), ser. 11 (sl. 30, line 2, sect. 4); Fig. 4*f*, fetus of 161 mm (19 wks.), ser. 13 (sl. 46, sect. 3); Fig. 4*g*, fetus of 183 mm (21 wks.), ser. 21 (sl. 46, sect. 3); Fig. 4*h*, fetus of 290 mm (32 wks.), ser. 59 (sl. 41, line 1, sect. 2).

Fig. 4*a*.—The manubrium of the malleus in the fetus of 16 weeks is still cartilaginous, but the long crus of the incus is surrounded by a perichondral shell (compare reconstruction, Fig. 8*f*). The ossification center is shown at increased magnification in Fig. 4*e*.

Fig. 4*b*.—In the manubrium of the infantile ear (here sectioned midlength) endochondral bone has been produced to such an extent that the remaining marrow cavity is very small. Remnants of intrachondrial bone are present.

Fig. 4*c*.—In the adult of 40 years, original cartilage persists on the exterior of the manubrium of the malleus, where it is immediately related to the enveloping tissue of the tympanic membrane. Periosteal bone is wanting.

Fig. 4*d*.—In the 16-week (117-mm) fetus the solitary ossification center appears on the anterior aspect of the long crus of the incus in the form of a thin layer of perichondral bone. Just beneath this lamina the cartilage gives initial evidence of ossification: the cartilage is being calcified, and the cells are increasing in size.

Fig. 4*e*.—In the ossification center of the incus (see Fig. 4*a*), in a fetus of approximately the same age ($16\frac{1}{2}$ weeks), erosion of the cartilage is taking place within the circumferential shell of bone. Periosteum gives rise to osteoblasts, which deposit a perichondral layer of bone; osteogenic buds, containing blood vessels, invade enlarging cartilage lacunae, some of which are already excavated; unaltered cartilage remains at deeper level.

Fig. 4*f*.—In the long crus of the incus, in the fetus of 19 weeks, periosteal bone has formed a complete shell, internal to which the marrow cavity is still a relatively extensive space. Some intrachondrial bone is present.

Fig. 4*g*.—In the long crus of the incus of a specimen two weeks older (21 weeks), endochondral bone has appeared as a thin, but as yet incomplete, layer, which is applied to the internal aspect of the perichondral layer. Some cartilage persists in association with the endochondral bone; intrachondrial bone is still present in the capacious marrow cavity. As a result of the continuing increase of endochondral bone, the marrow cavity will ultimately be obliterated.

Fig. 4*h*.—In the fetus of 32 weeks, the long crus of the incus is composed of a smooth outer layer of periosteal bone, and a much thicker inner portion composed of endosteal bone. A relatively small marrow cavity is still present. As yet there is no evidence of erosion of bone and, consequently, none of osseous restoration.

The extremity of the manubrium of the malleus remains cartilaginous (Fig. 1*c*).

The otic capsule, which, in the two preceding stages (183 mm and 190 mm), had attained adult dimensions, now has definitely entered the next phase of its developmental history—one in which an increment of periosteal investment will ultimately place the capsule at the core of the *pars petrosa* of the temporal bone. However, its middle layer (Fig. 1*c* at 2) is still sparse, and a considerable mass of the original cartilage remains in the canalicular division (compare adult specimen, Fig. 1*d*). The periotic spaces within the capsule are well formed. The tympanic cavity, relatively slow in its course of expansion, has not spread far enough medialward to envelop the incus or the stapes.

215-*mm fetus.* In the stapes of the fetus of 24 weeks, perichondral bone forms a complete layer except at the extremities of the ossicle; in each of these situations, cartilage remains as an intact lamina, but no longer as a mass (see head of ossicle, 202-mm fetus, Fig. 1*c*). The chondral lamina at the capital end is somewhat thicker than the one at the basal extremity. Endochondral bone forms an exceedingly thin covering for the latter; for the former it is as yet incomplete, occurring merely in the form of spicules. The obturator wall of the ossicle, now merely foraminous, is destined to be totally removed (see 380-mm stage, Figs. 3*a* and 3*b*).

At the distal extremity of the incus the cartilaginous portion has undergone further reduction in thickness.

The outer and inner layers of the otic capsule are well formed; however, the osseous tissue of the middle layer still consists of sparsely distributed intrachondrial bone, thus appearing as an excessively cancellous portion of the labyrinthine wall. Through the production of endochondral bone, deposited upon the intrachondrial framework, the capsule will ultimately attain petrous character (compare adult, Fig. 1*d*).

222-*mm fetus.* In respect to dimensions and to external appearance—with the exception of two features—the ossicles in the 25-week specimen are adult elements (Fig. 10*a*); these features are persistence of Meckel's bar and the cartilaginous state of the manubrium (Figs. 10*a* to 10*d*). Meckel's cartilage is now a more or less

amorphous remnant at the core of the anterior suspensory ligament of the malleus (Figs. 10*c* and 10*d*, 7*b* and 7*c*).

In both the head of the malleus and the body of the incus, endochondral bone now forms a layer of appreciable thickness to the perichondral layer (Fig. 7*b*). At this stage, formation of endochondral bone is further advanced in the long crus of the incus than it is in the proximal portion of the manubrium of the malleus.

In the incus, cartilage persists at the tip of the short crus where the latter is in contact with the otic capsule (Figs. 7*b* and 7*d*). Just internal to the cartilage which forms the apical part of the short crus, intrachondrial bone is present, and all stages in its conversion from cartilage are demonstrable (Fig. 7*d*). In more proximal position, perichondral bone, not cartilage, is the outer layer of the crus.

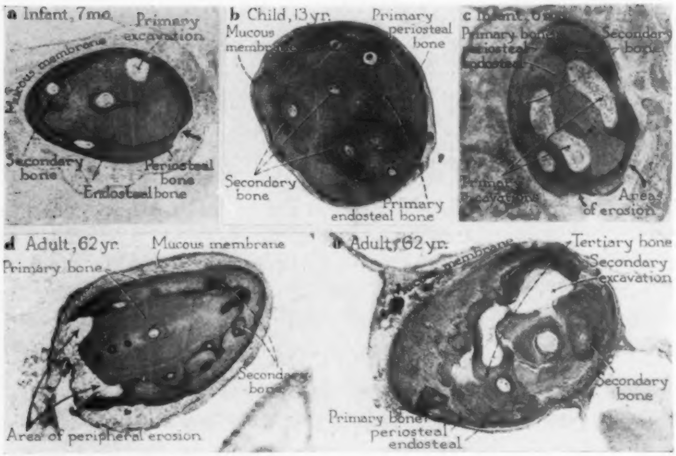
The anterior process of the malleus is closely related to the anterior suspensory ligament and to the tympanic ring (Fig. 6*e*).

243-*mm fetus.* The otic capsule of the 27-week fetus shows developmental advance over that of the 23-week (202-mm) stage in the greater thickness of the outer layer of bone (Figs. 2*a* and 2*b*; compare Fig. 1*c*). Unlike the external layer (Fig. 2*b* at 1), the inner one will remain unchanged; the endochondral bone of the middle layer has not yet been produced in appreciable amount.

In the long crus of the incus, endosteal bone now encloses a marrow cavity of decreasing size (Fig. 2*c*); the periosteal layer is similar to that of the crus in the fetus of 21 weeks, or 183 mm (Fig. 4*g*). The lenticular process is cartilaginous.

In the manubrium of the malleus, cartilage, not perichondral bone, is the outermost stratum of the long crus (Fig. 2*d*). Cartilage passes, by insensible histological gradation, into intrachondrial bone, spicules of which occupy a capacious marrow cavity (Figs. 2*b* and 2*c*).

The obturator wall of the stapes has not yet been completely removed. However, a thin layer of endosteal bone already lines the cartilaginous plates at the basal and capital extremities (Figs. 2*b* and 2*e*). Since the periosteal bone of the head, neck and base is still intact (except for foraminous openings), the primitive marrow remains undisturbed (Figs. 2*b* and 2*e*). Intrachondrial bone is almost nonexistent; were such tissue to be produced, its presence would be



Figs. 5*a* to 5*c*.—Photomicrographs of transverse sections through the long crus of the incus. Fig. 5*a*, X 33; Figs. 5*b* to 5*e*, X 30. Fig. 5*a*, infant of 7 months, ser. 120 (sl. 21, line 2, sect. 2); Fig. 5*b*, child of 13 years, ser. P4 (sect. 377); Fig. 5*c*, infant of 6 months, ser. B98 (sl. 36, sect. 6); Fig. 5*d*, adult of 62 years, ser. P10 (sect. 375); Fig. 5*e*, second adult specimen of the same age, ser. P13 (sect. 445).

Fig. 5*a*.—The long crus of the incus of the young infant (of 7 months) is already heavily osseous: the marrow cavity remains as a lesser space within an extensive field of endosteal bone. Even at this early stage, primary excavations have appeared; some of them are being filled by bone of haversian structure. Peripheral erosion has taken place in the areas indicated by the arrow.

Fig. 5*b*.—In the ear of a child (13 years of age), the histological structure of the incus resembles that of the ossicle in some early postnatal stages. This means that a state of quiescence may follow one in which primary excavations have been filled with secondary bone (compare preceding figure).

Fig. 5*c*.—In an example of incus from an infant 6 months old, there occur extensive excavations, the walls of which are just receiving lamellar applications of new bone.

Fig. 5*d*.—In some instances the long crus of the incus of the adult has passed through a single cycle of rebuilding; its architecture resembles that in the less altered ossicles of some infants. The periosteal layer may be locally eroded, as seen also in Figs. 5*a* and 5*c*.

Fig. 5*e*.—A third stage in remodelling of the incus is encountered in some adult specimens (in this instance, the same age as the preceding). Areas of erosion of the bone of secondary formation are being closed by production of new tissue (of tertiary order).

transitory, since the space thus occupied would soon be invaded by mucous membrane (compare 280-mm stage, Fig. 3*b*). The cartilaginous lamina on the vestibular aspect of the base is thin, but where such tissue is carried to the periphery of the base, it forms a flange-like rim. The apposed surface of the vestibular (oval) window is also cartilaginous (Fig. 2*e*). Normally, both will remain so throughout life.

Except for its relation to the obturator wall of the stapes (which is destined to be wholly removed), the reflection of the mucous membrane is essentially adult. Its spread in a four-week period (between the 202-mm and 243-mm stages) is one of striking rapidity (Fig. 2*b*; compare Fig. 1*c*).

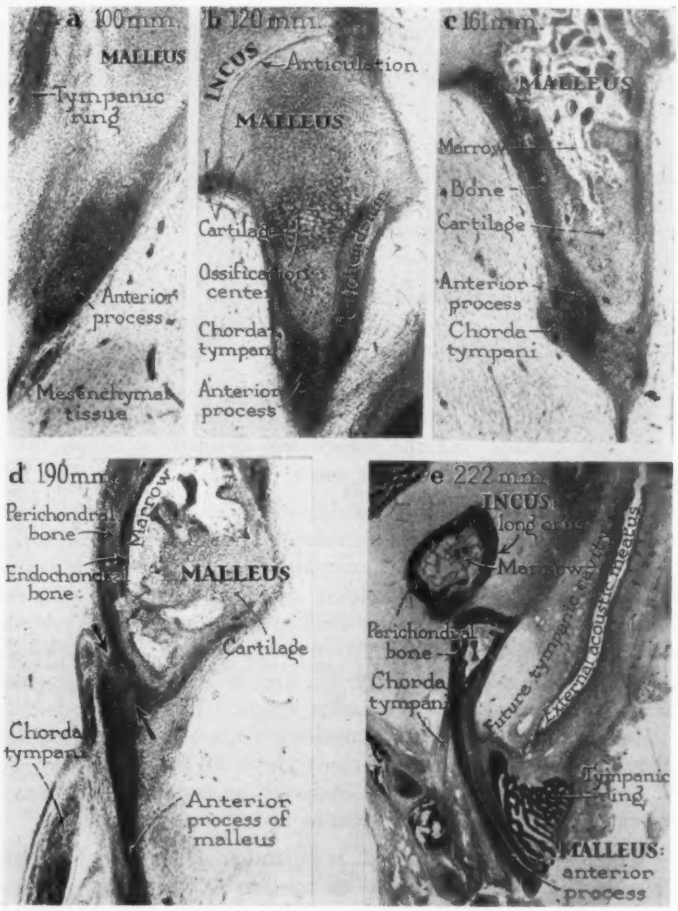
The tympanic ring, which begins to form shortly after the anterior process of the malleus, still remains largely independent of the osseous structures with which it will become fused (Fig. 2*a*).

280-*mm fetus.* In the succeeding four-week period (between the 243-mm and 280-mm stages) marked changes have taken place in the otic capsule and the stapes, less dramatic progress toward maturity in the malleus and the incus (Fig. 2*a*; compare Fig. 3*a*).

The otic capsule shows considerable advance in development; bone now approaches petrous character in both the cochlear and the canalicular divisions (Fig. 3*a*; compare Fig. 2*a*). In the latter part the facial nerve is almost completely surrounded by bone (Fig. 3*a*). The outer layer of the capsule is thicker than it was in the preceding stage. Endosteal bone, deposited upon the islands of intrachondrial bone, takes from the middle layer the highly "cancellous" appearance which characterized it in the earlier stages. Thus, so far as fabric is concerned, the capsule is approaching maturity; the internal layer will remain unaltered and the constituents of the other two layers will never be replaced by bone of haversian type. In this sense, it may be said that the capsule remains histologically primitive.

The long crus of the incus is bilaminar, both the perichondral and endochondral layers being of considerable thickness (Figs. 3*b* and 3*c*). As a result of the increase of endochondrial bone, the large marrow cavity of the incus in the 21-week fetus has become greatly reduced in the intervening period of ten weeks.

In the manubrium of the malleus, endochondrial bone has just appeared as a very thin layer (Figs. 3*b* and 3*d*). It is continuous internally with intrachondrial bone, externally with cartilage.


a 100mm.
MALLEUS
Tympanic ring
Anterior process
Mesenchymal tissue
b 120 mm.
INCUS
Articulation
MALLEUS
Cartilage
Ossification center
Chorda tympani
Anterior process
c 161mm.
MALLEUS
Marrow
Bone
Cartilage
Anterior process
Chorda tympani
d 190mm.
Perichondral bone
Marrow
Endochondral bone
MALLEUS
Cartilage
Chorda tympani
Anterior process of malleus
e 222 mm.
INCUS: long crus
Marrow
Perichondral bone
Chorda tympani
Future tympanic cavity
External acoustic meatus
Tympanic ring
MALLEUS: anterior process

Figs. *6a* to *6e*.—Photomicrographs of sections, in transversely cut series, of the anterior process of the malleus. Fig. *6a*, X 34; Fig. *6b*, X 27; Figs. *6c* and *6d*, X 36; Fig. *6e*, X 14. Fig. *6a*, fetus of 100 mm (15 wks.), ser. 22 (sl. 25, line 2, sect. 2); Fig. *6b*, fetus of 120 mm (16 wks.), ser. 56 (sl. 27, line 1, sect. 2); Fig. *6c*, fetus of 161 mm (19+ wks.), ser. 13 (sl. 55, line 1, sect. 3); Fig. *6d*, fetus of 190 mm (22 wks.), ser. 29A (sl. 30, line 1, sect. 3); Fig. *6e*, fetus of 222 mm (25 wks.), ser. 46 (sl. 53, line 1, sect. 3).

Fig. *6a*.—Although the malleus, incus and stapes are cartilaginous in the fetus of 15 weeks, the anterior process of the malleus, still an independent element, is fully formed in bone (see, also, reconstruction, Fig. 8*d*).

Fig. *6b*.—At a slightly later stage (fetus of 16 weeks, or 120 mm), the formation of periosteal bone has begun in the neck of the malleus, where the latter becomes continuous with Meckel's cartilage (first branchial arch); the anterior process is adherent to, but not yet fused with, the neck of the malleus (see, also, reconstruction, Fig. 8*e*).

Fig. *6c*.—In the fetus of approximately 19 weeks, periosteal bone invests the neck and head of the malleus (here sectioned at the transverse level of the incudomalleolar articulation); beneath the outer layer endochondral bone is being formed (see, also, reconstruction, Fig. 9*a*). The anterior process is now fused with the ventral margin of the neck of the malleus.

Fig. *6d*.—In a fetus 3 weeks older (22 weeks) than the specimen just described, the anterior process resembles a scimitar-like appendage of the malleus proper; the zone of fusion of the neck of the malleus with the appendange (at arrows) is still identifiable. Some cartilage persists within the malleus, although endochondral bone has appeared inside of the perichondral layer. Some islands of intrachondrial bone are present.

Fig. *6e*.—In the fetus of 25 weeks, the three ossicles have attained adult dimensions (see reconstruction, Fig. 10*a*). However, production of endochondral bone continues in the malleus and incus, ultimately to obliterate the marrow spaces (see Fig. 1*d*). The anterior process is intimately fused to the malleus.

The tympanic ring is still independent of the otic capsule (Fig. 3*a*).

The obturator wall of the stapes has been destroyed. Marrow has been replaced by mucous membrane except in the capital portion of the ossicle (Fig. 3*b*). The several portions of the stapes, as seen in sections, are excessively thin (Fig. 3*e*). Upon removal of the obturator wall, the stapes acquires superior and inferior crural arches along the margins of the hollowed members. In the basal portion of the ossicle, endochondral bone is spreading across the tympanic (lateral) surface of the persistent cartilaginous lamina of the base (Fig. 3*e*; compare Figs. 1*d* and 1*e*). Marginally the newly-formed bone encloses canals for transmission of blood vessels.

290-*mm fetus.* The long crus of the incus, in which endochondral bone was just beginning to form in the 21-week fetus (Fig. 4*g*), is now, in the 32-week fetus, an almost solid column of bone (Fig. 4*h*). The periosteal layer is no thicker than it was almost four months earlier at the midpoint in intrauterine development.

As described and figured in connection with earlier phases of this investigation, the stapes has attained adult dimensions while the remainder of the body is still fetal. The crura are converted into channelled columns, the head into an excavated cylinder with bilaminar articular extremity, and the base into a thin, two-layered plate. The several parts are excavated to expose their interiors circumferentially, at the expense of space which originally contained marrow and endochondral bone. The surface of bone thus exposed by erosion of the "diaphyseal" wall becomes covered by mucous membrane; blood vessels, now submucosal, communicate with others in the bone of the head, crura, and base.

Thus, unlike a regular long bone, the stapes lacks both cancellous tissue and marrow; during differentiation it sacrifices about one-half of its periosteal substance. Endochondral bone contributes negligibly to the bulk of crura and head, only moderately to that of its base. It grows as a cartilage, but fails to enlarge as a bone. The stapes differs further from a bone of typical intracartilaginous category in retaining on one surface, the vestibular, a broad plate of cartilage of nonarticular character.

Newborn. The articular process of the incus is little more than a ring of perichondral bone; some islands of intrachondrial bone are

scattered through its marrow, whereas the midportion of the long crus is formed of solid bone.

The distal extremity of the malleus is in the early stages of cartilage transformation. A thin and incomplete layer of endochondral bone, continuous with intrachondrial spicules, supports an external lamina of cartilage. Perichondral bone is wanting in the extremity of the manubrium not only during infancy but also in adult life (Fig. 4*c*).

Infants. During early infancy, the otic capsule assumes petrous appearance as a result of the rapid production of endochondral bone; by the application of additional periosteal lamellae during infancy and childhood, it will become deeply imbedded in the *pars petrosa* of the *os temporale.*[4]

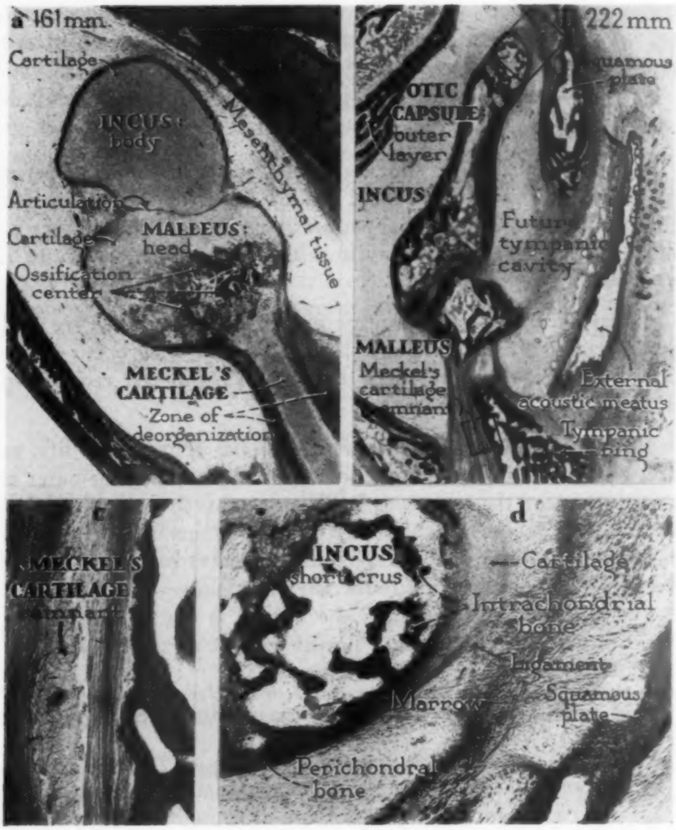
It has been observed that the malleus and the incus are somewhat unstable; internal and external remodelling may occur in these ossicles at any age, beginning in infancy. This matter requires special elucidation.

Even in an infant of the seventh month of postnatal life, evidences of remodelling are clearly seen: primary bone of the outer and inner portions of the long crus has been removed; new (secondary) bone of haversian type has filled the excavations (Fig. 5*a*). In a specimen of a 6-month infant, extensive excavations are just being reduced in expanse by the production of secondary bone (Fig. 5*c*). In some older infants, however, the process is not as far advanced, the structure of the part being similar to that of the 32-week fetus (Fig. 4*b*).

The manubrium of the malleus retains its investment of cartilage (Fig. 4*b*).

Children. In some examples of incus from the ears of children, the osseous tissue of the long crus is found to be in a quiescent state, following one of activity. In such specimens, secondary bone has completely filled prior excavations, and no further activity is evident (Fig. 5*b*). However, in other individuals of the same age, both primary and secondary bone is being removed for replacement by osseous tissue of tertiary order in the succession of changes.

Adults. Examples of incudal specimens from adults exhibit variabilities in constitution which exactly match those already de-


a 161mm.
Cartilage
INCUS: body
Mesenchymal tissue
Articulation
Cartilage
MALLEUS: head
Ossification center
MECKEL'S CARTILAGE
Zone of deorganization
222mm
Squamous plate
OTIC CAPSULE: outer layer
INCUS
Future tympanic cavity
MALLEUS
Meckel's cartilage remnant
External acoustic meatus
Tympanic ring
c
MECKEL'S CARTILAGE remnant
d
INCUS short crus
Cartilage
Intrachondrial bone
Ligament
Marrow
Squamous plate
Perichondral bone

Figs. *7a* to *7d*.—Photomicrographs of sections, in transversely cut series, of Meckel's cartilage and of the short crus of the incus. Fig. *7a*, X 17; Fig. *7b*, X 10; Figs. *7c* and *7d*, X 50. Fig. *7a*, fetus of 161 mm (19+ wks.), ser. 13 (sl. 62, line 1, sect. 3); Figs. *7b* to *7d*, fetus of 222 mm (25 wks.), ser. 46 (sl. 56, line 1, sect. 2).

Fig. *7a*.—In the fetus of 19 weeks, Meckel's cartilage is undergoing deorganization in the segment which is continuous with the malleus, and at a time when periosteal bone-formation involves only part of the neck and head of the ossicle (and even a smaller fraction of the incus). Distally (that is, toward the mandible), the cartilage is as yet unaltered (see reconstruction, Fig. *9a*).

Fig. *7b*.—Within less than 4 weeks, that is, in the 25-week stage, the deorganized part of Meckel's cartilage has been converted into ligamentous tissue (see reconstruction, Figs. 10*a* to 10*d*). In the short crus of the incus, cartilage persists in the area of ligamentous attachment. These two special regions, enclosed in blocks, are shown in detail in the following figures.

Fig. *7c*.—The degenerating remnant of Meckel's cartilage is lodged in the anterior ligament by which the former branchial element has already been largely displaced.

Fig. *7d*.—Showing the cartilaginous tip of the short crus of the incus and its ligament. The latter is in part attached to the squamous plate in the same specimen (see reconstruction, Fig. 10*a*), internal to which is situated intrachondrial bone, recently formed. The latter tissue has not become imbedded in bone of endochondral type.

scribed for the ossicle in both the infantile and the juvenile categories. Thus, it is possible to find in the long crus of a selected adult, structural features which virtually duplicate those of a slightly modified, or even unchanged, example from the ear of a young infant; and, conversely, infantile specimens are frequently encountered in which the original and fundamental histological pattern has been so profoundly altered that the degree of rebuilding would reasonably be associated with old age. Several specimens, selected from a large group, will serve to illustrate these points.

In some young adults, the architecture of the long crus of the incus gives less evidence of change than does the same part of the incus in an infant or in that of a child. In others, extensive excavation is taking place. While, in the light of these facts, still another cycle of removal and restoration of bone might be expected—and is actually encountered—in some older adults (Fig. 5*e*), others of the same age show little activity. Removal of bone is not limited to the interior of the crus in either the young or the old; the periosteal layer may undergo erosion in the infant (Fig. 5*c*), the child and the adult (Fig. 5*d*). There is, clearly, no time-limit set for this process of remodelling, since the authors have found the mechanism operative in the oldest specimens in their otological collection (adults past 70 years of age).

CONCLUSIONS

The auditory ossicles in man appear primordially as partial or complete derivatives of the mandibular (Meckel's) and the hyoid (Reichert's) cartilages. It will be recalled that these arches, first and second in the branchial series, form the boundaries of the first branchial groove, which is the forerunner of the external acoustic meatus; the otocyst, from whose epithelial wall will be derived the membranous (otic) labyrinth of the inner ear, is closely related to the arches.

From the beginning, the form of each of the primordial ossicles suggests, but in diminutive proportions, the shape of the adult bone to which it will give rise. Each ear-bone ossifies from a single center. All of them retain cartilage on their articular surfaces (incudostapedial and incudomalleolar). Cartilage is also retained on surfaces which, in some respects, resemble joints; for example, on the stapedial base, on the medial aspect of the short crus of the incus, and on the manubrium of the malleus.

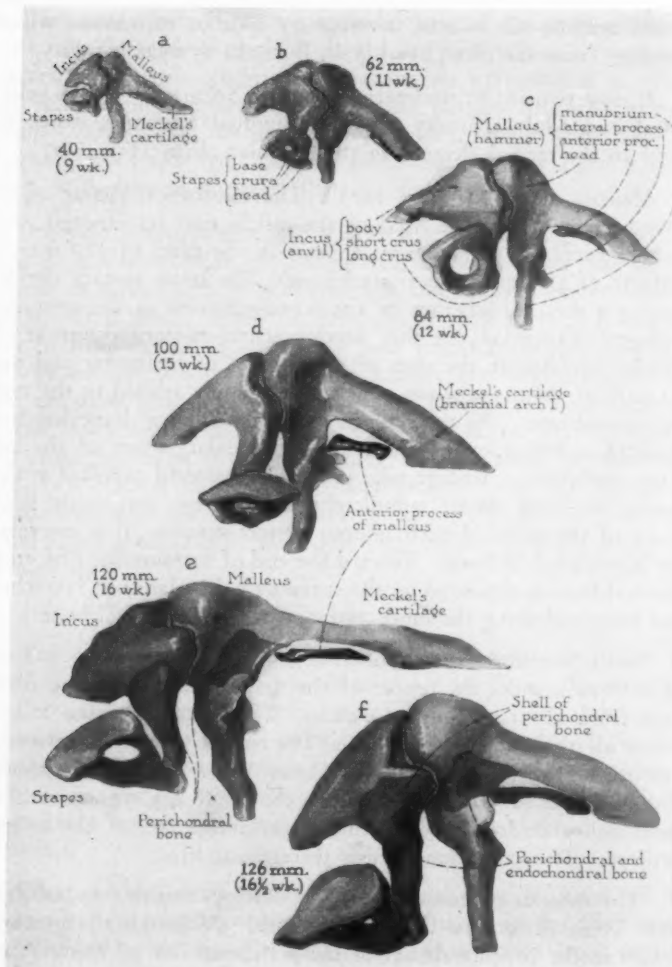
It is characteristic of the developing ossicles that growth ceases once perichondral bone is completely formed; all of them lack epiphyseal centers; all become invested by mucous membrane which, spreading from the pharyngeal wall, lines the tympanic cavity.

It now remains to summarize the chief features of the developmental and adult anatomy of the individual ear-bones, from the lateral to the medial element in the ossicular chain (Fig. 11*a*).

Malleus (*Figs.* 11*b and* 11*c*). The ossification center of the malleus is located on the head of the ossicle near its junction with Meckel's cartilage. The center appears in the fetus of 120 mm, in the form of a plaque of periosteal bone. The latter spreads rapidly, forming a shell, in advance of the transformation of the contained cartilage. Exceptions to this developmental pattern occur at the articular surfaces at the sites of attachment of ligaments and over that part of the manubrium which is intimately related to the tympanic membrane. As soon as the first perichondral bone has been deposited, calcification of the matrix and enlargement of the cells of the underlying cartilage take place. The altered cartilage is then invaded by, and almost completely replaced by, osteogenic tissue. If any of the calcified cartilaginous matrix remains, it is converted into intrachondrial bone. Toward the end of intrauterine life, endochondral bone is deposited on the surface of the islands of intrachondrial bone and along the inner aspect of the perichondral bone.

In the manubrium, perichondral ossification is wanting. Osteogenic tissue invades the center of the manubrium, spreading distalward from the neck of the ossicle. The invading tissue fails to remove all of the calcified cartilage. The remnants, when transformed into intrachondrial bone, are the bases upon which endochondral bone is deposited. In this way the center of the manubrium becomes endochondral bone, leaving a peripheral rim of the original cartilage. This condition persists throughout life.

The anterior process of the ossicle develops as a thin rod of membrane bone, present in the 28-mm stage. Although the process is located in the peripheral part of the perichondrium of Meckel's cartilage, it remains otherwise independent thereof. The anterior process is remarkably precocious in development, being formed in bone, in the 28-mm fetus, when the ossicles have just acquired definitive form in cartilage. Even at this early stage the process is almost as large as it is in the fetus of 120 mm, at which stage perichondral bone


a
Incus
Malleus
Stapes
Meckel's cartilage
40 mm. (9 wk.)
b
62 mm. (11 wk.)
Stapes base crura head
c
Malleus (hammer) manubrium lateral process anterior proc. head
Incus (anvil) body short crus long crus
84 mm. (12 wk.)
d
100 mm. (15 wk.)
Meckel's cartilage (branchial arch I)
Anterior process of malleus
e
120 mm. (16 wk.)
Malleus
Meckel's cartilage
Incus
Stapes
Perichondral bone
f
Shell of perichondral bone
Perichondral and endochondral bone
126 mm. (16½ wk.)

Figs. 8*a* to 8*f*.—Drawings of reconstructions of the auditory ossicles and Meckel's cartilage; viewed from the medial aspect. X 7.5. Fetal specimens, respectively, of 40 mm (9 wks.), 62 mm (11 wks.), 84 mm (12 wks.), 100 mm (15 wks.), 120 mm (16 wks.) and 126 mm (16+ wks.). Ser. 168, 160, 162, 22, and 11, respectively. Beginning with Fig. 8*e*, perichondral bone is indicated by the darker plaques; in Fig. 8*f*, and in the illustrations which succeed it (through Fig. 10d), endochondral bone is indicated by stippling.

Figs. 8*a* to 8*d*.—Stages in growth, through a 6-week period, from the 9-week to the 15-week stage (40 mm to 100 mm), prior to the beginning of ossification in the stapes, incus and main portion of the malleus. The anterior process (independent of the malleus and Meckel's cartilage) is, alone, formed in bone.

Fig. 8*e*.—In the fetus of 16 weeks, osteogenesis has appeared for the first time in the malleus and increased its spread in the incus. In the malleus the center of ossification is situated in the area of junction of the head and neck; in the incus, ossification begins on the long crus, in the stapes on the tympanic surface of the base. Each center consists merely of a shell of perichondral bone.

Fig. 8*f*.—In a slightly older specimen, excavation of cartilage (shown by stippling) has appeared beneath the previously formed pellicle of perichondral bone. Growth of the ossicles accompanies the progress of ossification, and will continue through the fifth month of intrauterine life.

is just beginning to form in the adjacent portion of the head of the malleus. The anterior process finally fuses with the malleus proper in the fetus of 161 mm, then appearing as a scimitar-like appendage along the caudal aspect of the relatively bulky first branchial bar (Meckel's cartilage). The early appearance of the anterior process as a well-developed osseous structure is matched by equally precocious formation of the tympanic ring.

Meckel's cartilage. The first bar of the primitive branchial skeleton, namely, Meckel's cartilage, is, in the 28-mm embryo, very large in relation to the size of the primordial ossicles. At that stage it is covered on its anterior aspect by the ossifying mandible. The growth of Meckel's cartilage keeps pace with that of the cartilaginous ossicles through the first seventeen or eighteen weeks of fetal life. Toward the end of this period, (or, more definitely, in the fetus of 161 mm) the tissue of the proximal (that is, malleolar) extremity of the bar undergoes deorganization. As a result, the constituent tissue is prepared for conversion into that of the anterior ligament of the malleus. So rapid is this change, that, within a six-week period (in the fetus of 222 mm), the cartilage remains merely as an amorphous core imbedded in heavily fibrous tissue.

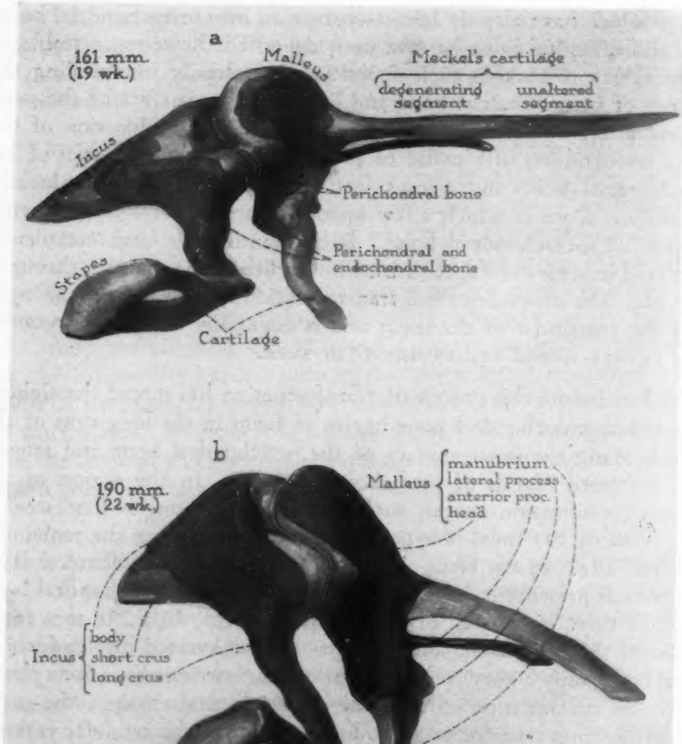
Incus (*Figs.* 11*d and* 11*e*). The earliest indication of ossification occurs in the incus in the fetus of 117 mm. At this stage, a peripheral plate of perichondral bone has formed on the anterior aspect of the long crus of the cartilaginous incus just beneath its fibrous covering. The cartilage, covered by the perichondral shell, shows the two early signs of osteogenesis: the cartilage cells have increased in size; the matrix has become infiltrated with calcareous deposits. Within a period of three days after the initiation of ossification, the perichondral bone has not only surrounded the midportion of the long crus of the incus but also has attained thickness almost equalling that of the adult. This condition obtains in the fetus of 126 mm. The envelope of perichondral bone spreads rapidly and, in stages between 190 mm and 222 mm, has virtually attained adult extent, forming an osseous investment for the incus, except for those limited areas which are either articular or which afford attachment for ligaments.

Although the perichondral bone attains mature dimensions at an early date, the original cartilaginous "model" contained within this perichondral bony shell in the form of a core is transformed into bone at a much slower pace. In the fetus of 126 mm, osteogenic

buds are invading the changing cartilage. In a fetus of 161 mm, the cartilage in the region of the ossification center has been completely replaced by osteogenic tissue except for a few small islands of cartilage which have already been transformed into intrachondrial bone. No endochondral bone has yet been deposited; however, osteoblasts, preparatory to making such deposition, are already surrounding the islands of intrachondrial bone and line the inner surface of the perichondral layer. Thus, at the 161-mm stage, the midportion of the long crus consists of a collar of periosteal bone, a few islands of intrachondrial bone and a considerable amount of centrally located osteogenic tissue in which a few osteoclasts are still actively removing islands of intrachondrial bone. Such islands have been completely replaced in some older specimens, while in others they remain throughout life. The above-described transformation spreads rapidly throughout the remainder of the incus and is essentially completed between the twenty-second and twenty-fifth week.

Just before this process of transformation has spread throughout the incus, endochondral bone begins to form in the long crus of the ossicle along the inner surface of the perichondral bone and around the scattered islands of intrachondrial bone. In the region of the original ossification center, such endochondral bone is first seen in the fetus of 183 mm; it is deposited gradually during the remainder of fetal life. In the fetus of 222 mm, a definite endochondral layer of bone is present; it forms a stratum beneath the perichondral layer and, in turn, is the wall of the marrow cavity. In a 290-mm fetus, most of the core of the long crus has been converted into endochondral bone; only a very small amount of marrow remains. Soon thereafter, in continuation of the same developmental changes, the entire incus becomes transformed into bone, except at the articular extremities and in areas of ligamentous attachment, where endochondral bone is covered by cartilage, not by perichondral bone. In these portions of the ossicle, endochondral bone is not covered by a perichondral layer. This condition will persist throughout life.

The osseous part of the incus is, in late fetal life, dense, consisting of a peripheral shell of perichondral bone and a central mass of dense endochondral bone. However, the incus is subject to rebuilding, a change which is effected through removal of bone in certain areas and by production of new bone in the parts thus excavated. The process is most striking as observed in the long crus. There is no specific age at which such primary reconstruction begins or ends;


a
161 mm.
(19 wk.)
Malleus
Meckel's cartilage
degenerating segment
unaltered segment
Incus
Perichondral bone
Perichondral and endochondral bone
Stapes
Cartilage
b
190 mm.
(22 wk.)
Malleus
manubrium
lateral process
anterior proc.
head
Incus
body
short crus
long crus
Stapes
base
crura
head

Figs. *9a* and *9b*.—Drawings of reconstructions of the ossicles, depicting stages in growth and differentiation of the ossicles; continued. Fetuses of 161 mm (19 wks.) and 190 mm (22 wks.). X 7.5. Ser. 13 and Ser. 29A.

Fig. *9a*.—In the 19-week fetus, perichondral bone has spread to the body of the incus and to the summit of the head of the malleus. Meckel's cartilage is concurrently undergoing decrease in size, the altered tissue becoming the anterior suspensory ligament of the malleus; the advance of endochondral bone is keeping pace with that of the perichondral layer. The anterior process of the malleus, hertofore independent, has fused with the cervical portion of the malleus. Perichondral bone envelops the basal ends of the stapedial crura.

Fig. *9b*.—Within a three-week period (in the fetus of 22 weeks), ossification in the incus has involved all of the ossicle except the articular portion and the extremity of the short crus; in the malleus, similarly, only the articular part and the manubrium remain cartilaginous; in the stapes, periosteal bone, advancing along the crura, has reached the neck of the ossicle. Adult dimensions have been virtually attained by the three ear-bones.

in some individuals it begins in fetal life and in others not until the person reaches advanced age. Primary resorption of bone has been observed in the 222-mm fetus, in the young child and in adults of advanced age. Likewise the refilling of the resorbed areas with bone may occur at various ages. Thus, in an infant of 6 months, a slight amount of secondary bone occurred at the peripheral portion of the excavated areas, whereas in a somewhat younger specimen (5 months) deposition of secondary bone was complete.

Rebuilding of the kind described is sometimes followed by further remodeling which, again, may occur at any age. Secondary erosion and subsequent deposition of tertiary bone has been noted in a child of 13 years, in an adult of 40 years, and in one 62 years of age. Comparison of two specimens 13 years old, and of two adults 62 years of age, demonstrates that the stage of rebuilding is not related to age. The fact is further emphasized by comparing the bones from specimens of widely different ages, such as an infant of 5 months and an adult of 62 years—in which only the primary perichondral and endochondral types of bone are present.

Stapes (*Figs.* 11*f* *and* 11*g*). Concerning the development of the stapes, the only features which warrant review are those which stand in contrast with the concurrent steps in morphogenesis of the malleus and incus.

Ossification is initiated later in the stapes (at about the 150-mm stage) than in either of the other two ossicles. However, bone-formation does spread from a solitary center—located on the obturator surface of the stapedial base. No sooner is the production of perichondral bone well under way, than erosion of the osseous shell begins, again on the obturator aspect of the ossicle. In the fetus of 170 mm, periosteal bone, rendered foraminous, surrounds the crura, extending from the base to the future neck of the stapes. In the 190-mm fetus the crura are converted into cylinders of bone, hollow except for the presence of a few spicules of calcified cartilage and intrachondrial bone in the cervical and basal portions. Endochondral bone has already spread across the capital end of the crural junction in the fetus of 183 mm. Adult dimensions have been attained. The process of erosion approaches completion in fetuses of 222 mm and 210 mm. The entire obturator wall has been removed in the 245-mm stage. The articular surface of the head and the vestibular surface of the base are now bilaminar, since the carti-

laginous plates have been completely lined with newly-formed endochondral bone. The ossicle of the 345-mm stage possesses the histologic structure and general conformation of the postnatal stapes. Mucous membrane, spreading with the expansion of the tympanic cavity, has replaced marrow tissue, thus coming to occupy continuously the base, crura and head of the ossicle on their facing (internal or obturator) surface.

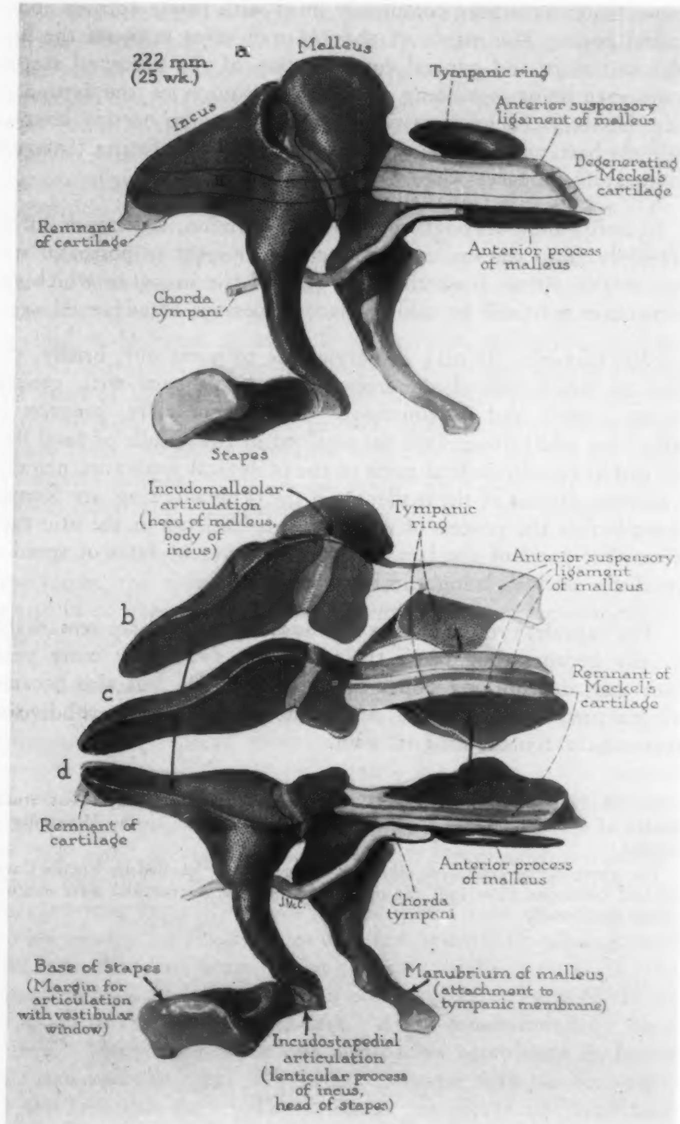
In losing bulk through the process of erosion, the stapes differs profoundly from the malleus and incus; in respect to postnatal stability, it also differs from the long crus of the incus, in which reconstruction may still be taking place in persons of advanced age.

Otic Capsule. It may be serviceable to point out, briefly, the degree to which ossicular morphogenesis keeps pace with general capsular growth and development. Both begin early, progress so rapidly that adult dimensions are attained in the middle of fetal life. And, just as certain skeletal parts of the otological apparatus, namely, the anterior process of the malleus and the tympanic ring, are formed in bone before the process of ossification is initiated in the otic capsule, so that parts of the latter mature at different rates of speed—that of the cochlea being the most rapid.

The capsule, tympanic ring and auditory ossicles are remarkable not only because they reach their full size twenty or more years earlier than do the long bones of the extremities, but also because, during a precocious course of development, each part or subdivision matures on a timetable of its own.

Mr. Shafik F. Richany prepared the reconstructions in support of studies presented in a thesis for the degree of Master of Sciences at the University of Wisconsin.

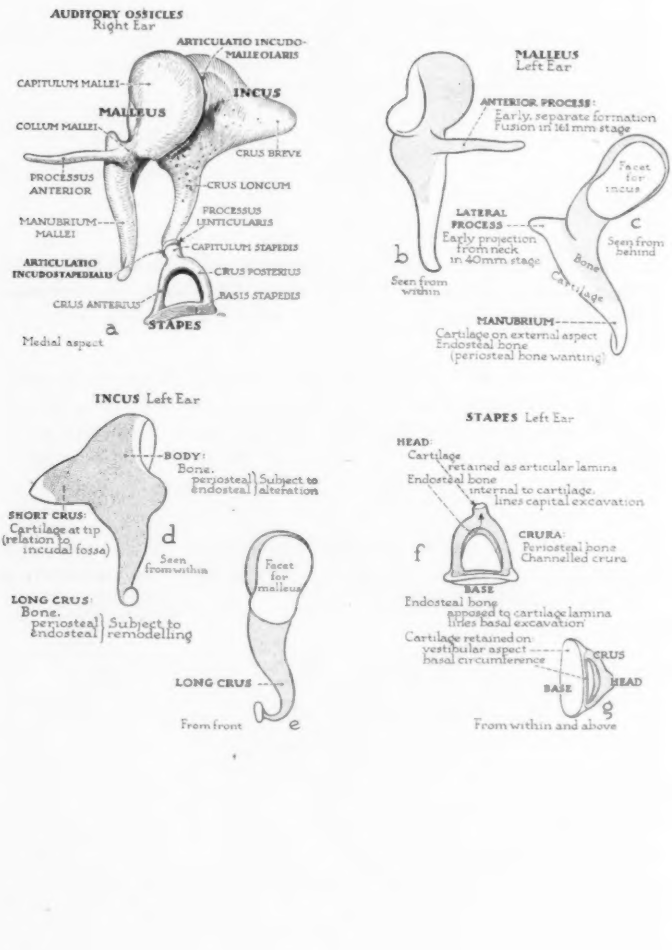
The photomicrographs were taken by Madge Walsh, labelled by Lucille Cassell Innes and Rosamond Howland; the drawings of the reconstructions were executed by Jean McConnell.


a
Malleus
222 mm.
(25 wk.)
Tympanic ring
Anterior suspensory ligament of malleus
Incus
Degenerating Meckel's cartilage
Remnant of cartilage
Anterior process of malleus
Chorda tympani
Stapes
Incudomalleolar articulation (head of malleus, body of incus)
Tympanic ring
Anterior suspensory ligament of malleus
b
c
Remnant of Meckel's cartilage
d
Remnant of cartilage
Anterior process of malleus
Chorda tympani
Base of stapes (Margin for articulation with vestibular window)
Manubrium of malleus (attachment to tympanic membrane)
Incudostapedial articulation (lenticular process of incus, head of stapes)

Figs. 10*a* to 10*d*.—Stages in the growth and differentiation of the auditory ossicles, shown by drawings of reconstructions; developmental stages concluded. Fetus of 222 mm (25 wks.). X 7.5. Ser. 46.

Fig. 10*a*.—In the 25-week (222 mm) fetus, bone-formation has made but moderate advance in the ossicles, but marked change is taking place in Meckel's cartilage; the cartilage itself remains only as a remnant within tissue which is being progressively converted into the anterior ligament of the malleus.

Figs. 10*b* to 10*d*.—The relations of the cartilage and the ligament of the same specimen shown by separating the portions of the reconstruction (segmentally marked in Fig. 10*a*).


AUDITORY OSSICLES
Right Ear
ARTICULATIO INCUDO-MALLEOLARIS
CAPITULUM MALLEI
INCUS
MALLEUS
COLLUM MALLEI
CRUS BREVE
PROCESSUS ANTERIOR
CRUS LONGUM
PROCESSUS LENTICULARIS
MANUBRIUM MALLEI
CAPITULUM STAPEDIS
ARTICULATIO INCUDOSTAPEDIALIS
CRUS POSTERIUS
CRUS ANTERIUS
BASIS STAPEDIS
a
STAPES
Medial aspect
MALLEUS
Left Ear
ANTERIOR PROCESS:
Early, separate formation
Fusion in 161 mm stage
Facet for incus
LATERAL PROCESS
Early projection from neck in 40mm stage
c
Seen from behind
b
Seen from within
Bone
Cartilage
MANUBRIUM
Cartilage on external aspect
Endosteal bone
(periosteal bone wanting)
INCUS Left Ear
BODY:
Bone.
periosteal } Subject to
endosteal } alteration
SHORT CRUS:
Cartilage at tip
(relation to incudal fossa)
d
Seen from within
Facet for malleus
LONG CRUS:
Bone.
periosteal } Subject to
endosteal } remodelling
LONG CRUS
From front
e
STAPES Left Ear
HEAD:
Cartilage
retained as articular lamina
Endosteal bone
internal to cartilage.
lines capital excavation
CRURA:
Periosteal bone
Channelled crura
f
BASE
Endosteal bone
apposed to cartilage lamina
lines basal excavation
Cartilage retained on:
vestibular aspect
basal circumference
CRUS
HEAD
BASE
g
From within and above

Figs. 11*a* to 11*g*.—The auditory ossicles, with summarizing notations on major features in the developmental anatomy of each. (See Conclusions.)

Fig. 11*a*, after Sobotta-McMurrich; Figs. 11*b* to 11 *g*, modified from Gray. The position of view is indicated in each figure.

Figs. 11*b* and 11*c*.—The notable features in the development of the malleus are the following: precocious, independent, development of the anterior process, its ultimate fusion (in the 19-week fetus) with the neck of the ossicle; early formation of the lateral process as a projection of the ossicle itself; retention of cartilage (in the absence of perichondral bone) as the outer layer of the manubrium in its distal portion.

Figs. 11*d* and 11*e*.—In the case of the incus, the remarkable features in morphogenesis are two in number; malleability of structure of the ossicle, expressed in a process of histological remodelling which may continue into old age or terminate in childhood; retention of cartilage at the apex of the short crus of the incus, where the latter is held by ligamentous tissue to the wall of the incudal fossa.

Figs. 11*f* and 11*g*.—The stapes is remarkable for three features of development: the manner in which the entire ossicle becomes channelled on its obturator aspect; the way in which endosteal bone comes to cover the internal aspect of the cartilage plates which have been retained, from fetal stages, at the capital and basal extremities; the replacement of primitive marrow, circumferentially within the hollowed ossicle, by mucous membrane of the tympanic cavity.

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XXXVI

CAPILLARY AREAS OF THE MEMBRANOUS LABYRINTH

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The tendency in recent years to relate numerous manifestations of cochlear and vestibular dysfunction to vascular disturbances has created a renewed interest in circulatory studies of the inner ear. Several comprehensive studies of the blood supply to the labyrinth have been made. The first was made by Siebenmann for the human labyrinth in 1894.[1] Asai[2, 3] followed in 1908 with a comparative study of the dog and the rat. Nabeya[4] in 1923 made a similar study of the guinea pig, cat, dog, monkey and human.

There has been some disagreement as to the similarity of vascularization between the species. Asai[3] believed the dog, rat and human showed an identical vascularization, with variations of a secondary character. Nabeya concluded the blood supply of the human labyrinth was remarkably different from that of other mammals except the monkey. These studies have emphasized the larger features of blood supply. More recently Scuderi and Del Bo's[5] studies of the capillary areas of the human ear show a considerable similarity to those of the guinea pig.[6]

The guinea pig and the cat have been used extensively in research programs that deal with electro-physiology, studies in acoustic trauma, observations concerning drug action, as well as circulatory studies. The value of the clinical application of these experimental results to man is related to the similarity of structure and function in the three species. The circulatory system is an important part. The present studies represent a comparative analysis of the capillary areas in the cochleas of the guinea pig, the cat and the human.

MATERIALS AND METHODS

Observations were made on eight cats. In most of these the blood vessels were studied after the intravascular precipitation of

Supported by a grant from the Central Bureau of Research of the American Otological Society.

Prussian blue or lead chromate by methods previously described.[6] Following dehydration and clearing, pieces of the membranous labyrinth of the cochleas were dissected out and examined. One ear was stained by the benzidine method. Sections of celloidin embedded ears were also studied.

The human material consisted of ears removed at autopsy from five full-term newborn infants, and one premature infant (about 6 fetal months). The petrous bones were removed and immersed in either Heidenhain-Susa fixative for 18-24 hours, or 2 per cent sodium chloride in 10 per cent formalin solution for one to several weeks. Pieces of the membranous labyrinth were dissected from the cochlea and stained by the benzidine stain. The technique followed for the benzidine stain was that given by Doherty, Suh and Alexander,[7] with some modifications.

1—Wash the pieces of tissue in distilled water for 30 minutes.

2—Stain in the following solution for 30 minutes at 37° C.:
 0.5 gm benzidine in 50 ml absolute alcohol
 0.1 gm sodium nitroprusside in 50 ml distilled water
 Dissolve and mix

3—Wash briefly in distilled water.

4—Stain in the following solution until the blood vessels appear black against a colorless background. This usually takes about 30 minutes at 37° C.
 50 ml absolute alcohol
 2 ml glacial acetic acid
 0.5 ml 30 per cent hydrogen peroxide
 0.1 gm sodium nitroprusside
 Distilled water to make 100 ml.

5—Wash in distilled water.

6—Dehydrate in 80 per cent and 95 per cent alcohol (with 2 per cent glacial acetic acid), and 100 per cent alcohol (without the acid).

7—Clear and mount.

Sections of celloidin embedded ears from eleven individuals of 2½ months to 56 years of age were also examined.

FINDINGS

The capillary areas of the membranous labyrinth of the cochlea are found in the spiral ligament and the spiral lamina. Observations

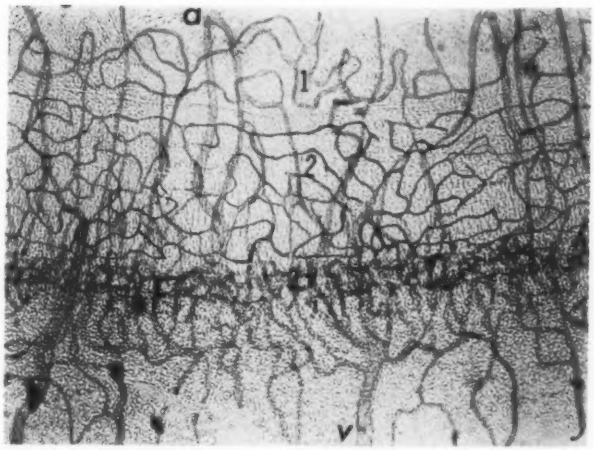

Fig. 1.—Photomicrograph of dissected specimen of spiral ligament from the cat cochlea. Intravascular precipitation of Prussian blue; magnification 100 x. *a*, arteriole; *v*, venule; *1*, network in the upper spiral ligament; *2*, network in the stria vascularis; *3*, network in the spiral prominence.

on these areas have been previously made of the guinea pig.[6] These studies include observations of the same areas of the cat and the human.

THE CAT

Spiral Ligament. The vascular pattern in the spiral ligament of the cat cochlea is similar to that of the guinea pig with some variations. The arterioles radiate from the modiolus out over the scala vestibuli in the bony partition and divide in the upper spiral ligament. They make their final ramifications lateral to the stria vascularis. Four capillary groups may be identified, according to course and location: the vessels in the upper spiral ligament, in the stria vascularis, in the spiral prominence, and the straight vessels in the deeper part of the spiral ligament.

Small branches of capillary size can be seen in the upper spiral ligament bordering the scala vestibuli (Fig. 1). These form a narrow network above the stria vascularis. Small vessels continue down

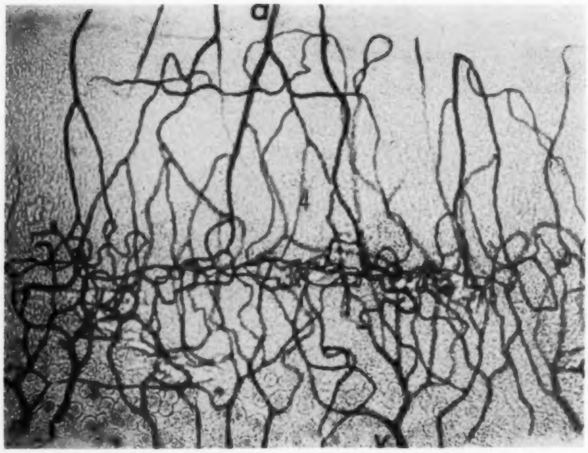

Fig. 2.—Photomicrograph of dissected specimen showing vascularization of the spiral prominence in the cat cochlea. Strial network not injected. Intravascular precipitation of Prussian blue; magnification 100 x. *a*, arteriole; *s*, sub-mesothelial capillary of the lower spiral ligament; *v*, venule; *3*, network of the spiral prominence; *4*, straight vessels in the thicker part of the spiral ligament.

from the network through the thicker part of the spiral ligament and enter the venules below.

The network of the stria vascularis is a wide, flat capillary mesh, continuous from base to apex (Fig. 1). It is supplied by large arteriolar branches. Large veins drain it. These are usually alternating and equivalent in number. No other connections with the vessels of the spiral ligament were noted.

Large branches turn into the spiral prominence. A narrow rolled network of capillaries coursing in the spiral direction fills in the spiral prominence and continues into the area lateral to it (Fig. 2). Numerous vessels turn lateralward from the prominence to enter the venules in the lower spiral ligament.

The final ramifications of the radiating arterioles may be in the thicker part of the spiral ligament, lateral to the stria vascularis

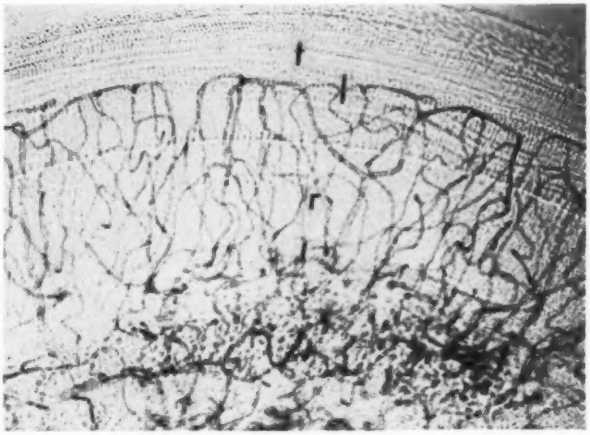

Fig. 3.—Photomicrograph of dissected specimen showing vessels in the labium tympanicum of the spiral lamina of the cat cochlea. No vessel is present below the tunnel of the organ of Corti. Intravascular precipitation of Prussian blue; magnification 100 x. *t*, tunnel of the organ of Corti; *l*, labium tympanicum; *r*, Rosenthal's canal.

(Fig. 2). The straight vessels that descend directly to the venules are found here.

The venules which receive the blood from all the groups of vessels in the spiral ligament are found adjacent to the scala tympani. Small venules predominate. A few small vessels can also be seen winding in the spiral direction just below the mesothelium. These are usually branches of the straight, direct vessels of the spiral ligament (Fig. 2). The larger venules cross the floor of the scala tympani to end in the large modiolar veins.

Spiral Lamina. Two groups of capillaries which terminate as looped spiral borders are visible in the spiral lamina. One is found in the limbus where it forms a looped sub-epithelial border at its edge. These vessels sometimes turn down and continue out toward the organ of Corti. More often they join the venules in Rosenthal's canal.

The other group of vessels course outward with the nerve fibers in Rosenthal's canal. They leave the bone below the internal spiral

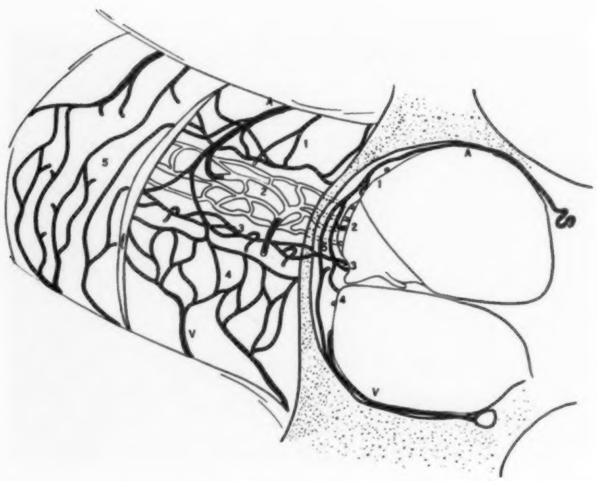

Fig. 4.—Schematic drawing showing typical distribution of small blood vessels in the spiral ligament of the human cochlea. The thicker part of the spiral ligament has been removed in the right half of the turn to expose the more superficial vessels. *a*, arteriole; *v*, venule; *1*, network of the upper spiral ligament; *2*, network of the stria vascularis; *3*, network of the spiral prominence; *4*, network of the lower spiral ligament; *5*, straight vessels in the thicker part of the spiral ligament.

sulcus and form a discontinuous spiral border in the labium tympanicum (Fig. 3). Sometimes they continue outward to form a third border below the tunnel of the organ of Corti. In six of the eight cats examined, no vessel was present under the tunnel. Generally, the arterial branches are near the upper or vestibular bony plate, and the venular vessels closer to the tympanic plate, but this is not a constant finding.

In some of the cats, the region of the round window was particularly studied. At the mouth of the cochlear aqueduct there is a shallow depression in the bone filled with loose connective tissue. Small vessels, some of capillary calibre, can be found here. In two cats these small vessels showed anastamoses with the venules of the scala tympani. It was further noted that a vessel crossed the round window membrane from the middle ear to the vein of the cochlear aqueduct.

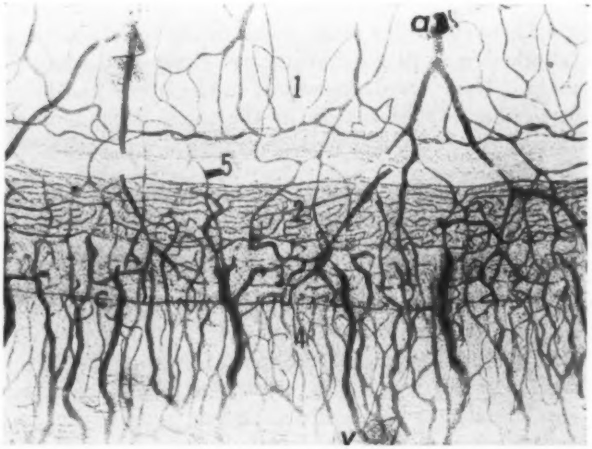

Fig. 5.—Photomicrograph of dissected specimen of spiral ligament from the human cochlea. Benzidine stain; magnification 45 x. *a*, arteriole; *c*, vessel in the crest of the spiral ligament; *v*, venule; *1*, network in the upper spiral ligament; *2*, network in the stria vascularis; *3*, network in the spiral prominence; *4*, network in the lower spiral ligament; *5*, straight vessels in the thicker part of the spiral ligament.

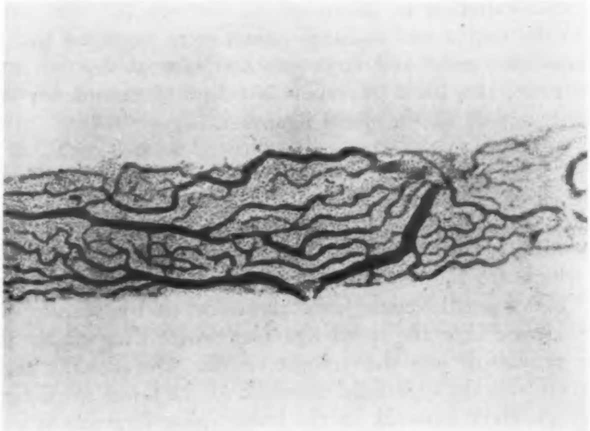

Fig. 6.—Photomicrograph of dissected piece of stria vascularis from the human cochlea. Benzidine stain; magnification 80 x.

THE HUMAN

Spiral Ligament. The small vessels in the spiral ligament of the human labyrinth may be divided into five groups according to course and location. These are the networks in the upper and lower spiral ligament, in the stria vascularis, in the spiral prominence and the straight vessels in the thicker part of the spiral ligament (Fig. 4).

The arterioles which radiate out over the scala vestibuli leave their bony canals at the upper limits of the spiral ligament and give off several large branches. At least one of these turns in the spiral direction above the attachment of Reissner's membrane and joins with similar branches from other arterioles. These form a large vessel above and parallel to the stria vascularis. A network originates from it and spreads upward in the spiral ligament (Fig. 5). Many of the capillaries are found just below the mesothelium, but some also extend lateralward to the bone. A few vessels turn downward from the network to end in the venules of the lower spiral ligament, but this network apparently drains for the most part into the veins that are found over the scala vestibuli in the human. The width of the network varies directly with the variation in the size of the spiral ligament from base to apex.

The capillaries of the stria vascularis form a flat network extending from vestibule to apex (Fig. 6). These specimens showed considerable variation in distension of the vessels. The capillaries closest to the source and drainage points were engorged with blood. Large arterioles enter and large venules leave at regular intervals. In most cases, this band of vessels is otherwise completely separate from other vessels of the spiral ligament.

The vessels in the spiral prominence form a separate, narrow rolled network below that of the stria vascularis continuous in the spiral direction (Fig. 7). Large arteriolar vessels enter it (Fig. 8). The network is formed by the interconnections between the spiral vessels which are found close to the epithelium bordering the scala media. Many small vessels leave the network by turning upward and lateralward into the spiral ligament where they empty directly into the venules or join the straight vessels. Occasionally they continue down into the superficial network of the lower spiral ligament.

The capillary network in the lower spiral ligament is also supplied by direct large arteriolar branches (Fig. 8). These descend close behind the stria vascularis and, after giving off branches to the

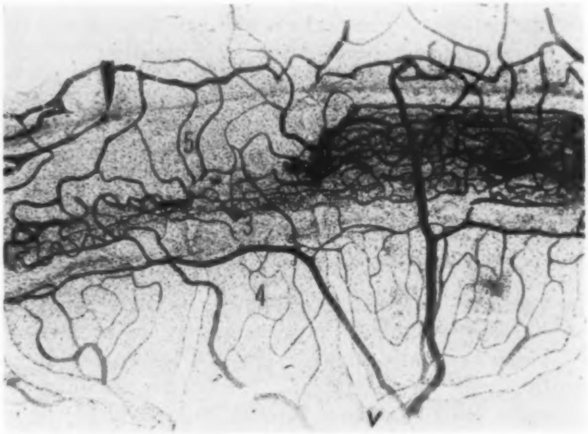

Fig. 7.—Photomicrograph of dissected specimen of spiral ligament from the human cochlea. The stria vascularis has been removed from the left half of the specimen to emphasize the network of the spiral prominence. *v*, venules; *3*, network in the spiral prominence; *4*, network in the lower spiral ligament; *5*, straight vessels in the thicker part of the spiral ligament.

stria vascularis and spiral prominence terminate in a spiral vessel in the crest of the spiral ligament. This vessel is not continuous and may even be double. It marks the upper limits of a network that originates from it, and is perpendicular to it (Figs. 5 and 8). In the apex, where the spiral ligament is thin, this network is seen as a simple, loose mesh of vessels under the mesothelium of the scala tympani. In the basal turn, the network extends laterally into the thicker part of the spiral ligament.

Besides these networks, the straight vessels that course more or less directly between arteriole and venule are found in the connective tissue between the scalae and the bone. In th upper part of the cochlea, they are shorter and straighter than in the basal turn. They show variations in size and structure. Some are undoubtedly capillaries with no apparent perivascular cells. Others are larger and may represent a kind of arterio-venous shunt such as has been described in most other places of the body (Figs. 5 and 7).

Spiral Lamina. The arterioles destined for the spiral lamina enter Rosenthal's canal and reach out toward the organ of Corti with the radial nerve fibers. The nerve is well vascularized and the larger vessels appear to course in between the nerve bundles.

The arteriolar branches on the vestibular side of Rosenthal's canal form a spiral vessel medial to the attachment of Reissner's membrane from which the vessels of the limbus originate. Vessels of capillary size are also sometimes seen in this location just below the mesothelium. A capillary border can be found at the edge of the limbus below the epithelium. Vessels from it continue down through the nerve fibers to the labium tympanicum.

The vessels in the outer compartment of Rosenthal's canal, plus the vessels from the limbus continue lateralward to form a plexus in the labium tympanicum (Fig. 9). Two discontinuous spiral borders can usually be identified. One is near the inner hair cell. The outermost border is found beneath the tunnel of the organ of Corti. Some vessels may loop out under the pars pectinata of the basilar membrane. In several ears, there were connections with the vessel in the crest of the spiral ligament. This was found more often in the apex. The venules turn back, usually into the bone, and can be seen in the spaces between the bone and nerve fibers.

DISCUSSION

Th distribution of small blood vessels in the cochleas of the three species is greatly similar. The arterioles radiate out from the modiolus over the scala vestibuli and ramify in the spiral ligament. Some of the branches turn in a spiral direction above Reissner's membrane and form either a simple or an extensive network in the upper spiral ligament. The stria vascularis is a separate capillary network with arterioles entering and venules leaving it at intervals. A single vessel or simple network is found in the spiral prominence. Some small vessels which many be expanded into a network are found in the lower spiral ligament. There are some vessels in the thicker part of the spiral ligament coursing more or less directly from arteriole to venule.

In the spiral lamina, the vessels in the limbus form a sub-epithelial spiral border at its edge. The radiating nerve fibers in their bony compartments are well vascularized. The capillary field terminates laterally as a plexus in the labium tympanicum which may extend out to the tunnel of the organ of Corti.

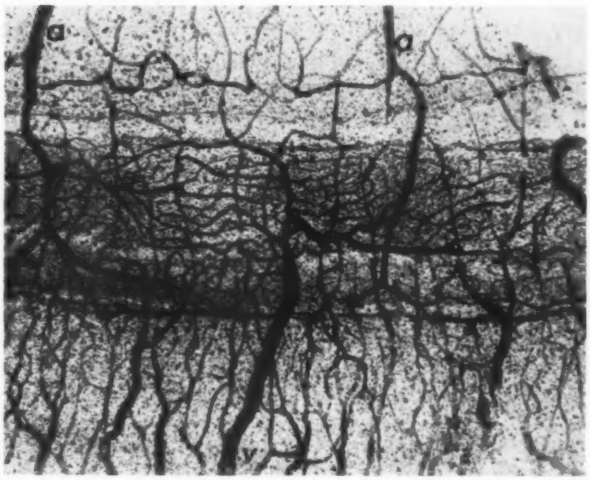

Fig. 8.—Photomicrograph of dissected specimen of the spiral ligament from the human cochlea showing large arteriolar branches entering the various capillary groups. Benzidine stain; magnification 100 x. *a*, arteriole; *v*, venule.

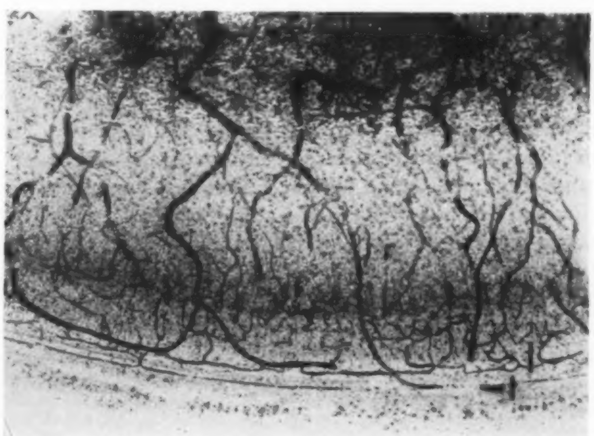

Fig. 9.—Photomicrograph of dissected specimen of spiral lamina from the human cochlea. Benzidine stain; magnification 100 x. *l*, labium tympanicum; *r*, Rosenthal's canal; *t*, tunnel of the organ of Corti.

There are some variations, but these seem to be mostly of a secondary character related to structural differences between the species. That part of the spiral ligament adjacent to the scala vestibuli and scala tympani is much wider in the human than in the cat and guinea pig. The few superficial vessels found there in these animals are expanded into networks in man. The low spiral prominence of the guinea pig contains but a single spiral vessel, while a network of vessels is found in the larger prominence of the cat and man. Even in the same animal, regional variations are always evident. The apical turn, where the spiral ligament is smaller, always exhibits a simpler vascularity than the basal turn. At the apex, the networks in the upper and lower spiral ligament are restricted to a single layer. The arterio-venous arcades are short and straight. In the basal turn, these networks extend lateralward into the thickness of the ligament; the straight vessels are branched and more complex.

The vessel below the tunnel of the organ of Corti has often been emphasized when referring to the blood supply of the organ of Corti. Its position as the vessel closest to the hair cells has undoubtedly directed attention to it. The frequent absence of the vessel in the cats makes one question its importance. Its variability in other species has been noted before.[8] It seems likely that it is only a part of the vascular plexus of the labium tympanicum and has little, if any, significance alone.

One finding that is more obvious in the cochlea of the human than in that of the other mammals is the definite arteriolar supply of the various vascular groups of the spiral ligament. The spiral ligament does not show one large continuous capillary field such as seems apparent in the spiral lamina, but rather several distinct capillary groups. The networks in the stria vascularis, the spiral prominence and the upper and lower spiral ligament are separated by vascular supply and drainage. Such a pattern greatly favors the possibility of regional circulatory variations within even a small segment of the spiral ligament. Not only is it probable that there are differences in pressure and velocity of flow[9] but circulatory disturbances may be found in one place without necessarily being present elsewhere.

No complete theories of the circulation of perilmph and endolymph can be formulated from studies that do not include the vestibular labyrinth. It seems possible, however, that perilymph is

formed and resorbed in the cochlea partly by the capillaries in the spiral ligament. The superficial networks in the upper and lower spiral ligament must play an important part. As the spiral ligament seems to be more or less permeable to perilymph,[10] it is probable that the vessels in the depths of the ligament also contribute. The capillaries in the labium tympanicum must also be included. It seems reasonable to assume that perilymph is formed and resorbed in both scalae in the cochlea by the capillaries in the spiral ligament and the spiral lamina.

SUMMARY

The distribution of small vessels in the spiral ligament and spiral lamina of the cochleas of the guinea pig, cat and the human is very similar. Some differences have been observed, but these seem to be secondary in character, related to species variations in structure.

EUCLID AVE. AND KINGSHIGHWAY BLVD.

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XXXVII

SOME ELECTRO-MECHANICAL PROPERTIES OF THE ORGAN OF CORTI

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Since Helmholtz wrote his famous book, "Die Lehre von den Tonempfindungen," in 1863, the question of frequency analysis in the cochlea has always been in the center of interest. His resonance theory of hearing gave a common point of view to a large variety of phenomena in the field of physiology, psychology and music and was highly stimulating in all these fields. Unfortunately it did not satisfy the specialists, and consequently a large number of hearing theories have been developed since that time. My opinion is that the frequency analysis in the cochlea is a question that cannot be answered today and I see no reasons why this cannot be stated explicitly. I think it is a mistake to force the answer to a question. As I see it, the difference between successful and unsuccessful research is basically a problem of asking the right question. I can distinguish the following types of questions:

(1) The unimportant question.

(2) The premature question.

(3) The strategic question.

(4) The stimulating question.

(5) The embarrassing question (the kind that is asked at meetings).

(6) The pseudo-question (often a consequence of a different definition or a different approach).

As a beginner I wanted to find a strategic question but I was unable to do so. It was an economist who asked me the first reasonable question in the field of hearing. I would like to tell you how it happened, because I think it will interest you to learn how a physicist gets involved in physiology.

The economist I mentioned was responsible for the development of the communication networks of the government. His question was: "Can a major improvement of the quality of communication systems be expected in the near future?" To answer this question I first compared the quality of the different parts of the communication systems to find the weakest point in the system. It was easy to show experimentally that the receiver was by far the weakest link in a transmission line. The next question was: "How much worse is a receiver than the ear?" I have no means of judging the quality of the inner ear, but the ear drum with the ossicles seems to be so similar to the mechanical part of a receiver that I decided to compare the transmission properties of the ear drum with the transmission properties of the diaphragm of the receiver. At that time I expected the receiver diaphragm to be much better fitted to the transmission of speech than the ear drum with its attached ossicles.

A quick way to determine the mechanical properties of a vibrating system is to give the system a sharp push and then register its oscillations. If you pull a string you have an oscillation with decreasing amplitudes, and from the decay curves you can determine the resonant frequencies of the string and their damping, which gives a complete description of the mechanical properties of the string. It is easy to pull the diaphragm of a receiver with a very short electrical pulse sent through the coils of the receiver The time pattern of the oscillations of a receiver diaphragm (telephone type receiver) is shown in Figure 1b. It is obvious that the long decay time of the oscillations distorts the speech sounds. Now the next question was, are the oscillations of the ear drum just as bad?

I decided that I would try to glue small mirrors onto the ear drum and then register with a light beam the oscillations produced by a sharp click. To produce a click the discharge of a condenser through a spark was appropriate. My biggest problem was the preparation of the temporal bone with the openings for the light beams. At that time the surgeons used a chisel and hammer to work on the bone. They are probably good for living objects, but in a preparation used for measurements some cracks may change the results. Therefore I used a dental drill. As seen in Fig. 2 the tip of the drill consisted of a small tube which made openings about 5 to 8 mm in diameter without the need of big forces. The openings were so precise that small brass tubes with glass windows could be fitted in airtight. The main problem was to have the windows in the right

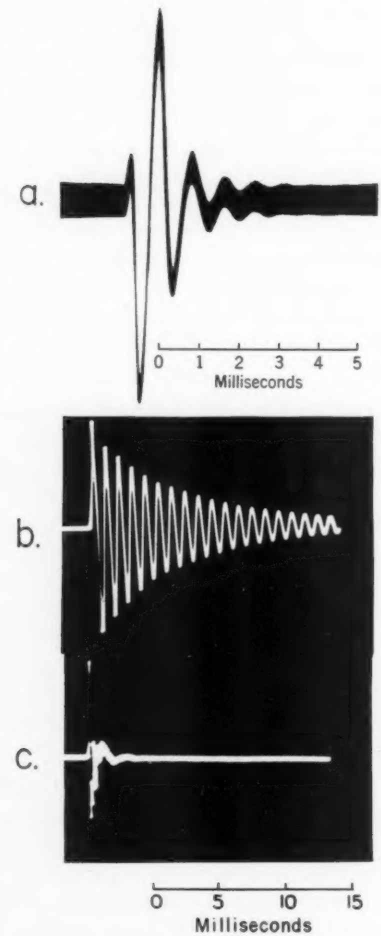

Fig. 1.—(a) The free oscillations of the human ear drum, (b) the oscillations excited in the earphone diaphragm by the pulse, and (c) the free oscillations of a modern earphone. This pattern of the free oscillations shows that the ear drum was much better a few years ago than earphones with regard to the fidelity of the transmission of speech sounds.

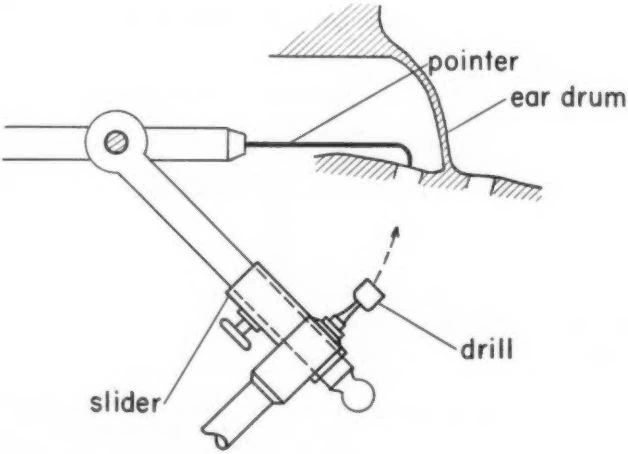

Fig. 2.—Equipment to drill holes quickly in a preparation of the human temporal bone. A pointer is put on the spot where the hole is wanted. By the pressing together of two arms of a forceps, a drill is moved toward the pointer. In this way, in the absence of anatomical knowledge, holes just before and just behind the ear drum can be made within a few seconds. They are all the same size so that a tube with a glass window can be easily fitted into the holes.

place so that the light beam could go through the glass window. To achieve this the drill was mounted on one arm of a forceps, which had a pointer on the other arm. This pointer was put at the spot in the meatus where the opening had to be made, and by compressing the forceps the drill and the point came together, as shown in the figure. If an opening in the middle ear was wanted, the position of the drill on the arm of the forceps was displaced to the periphery about 5 mm, and the forceps with the rotating drill was compressed again. The opening was now just behind the ear drum. The temporal bone and the rotating axis of the arm of the forceps were clamped together on a solid stand and this made the whole procedure so simple that the preparation could be done in 5 to 10 minutes. To measure the movements of the ear drum small mirrors were glued on the malleus. Control experiments had to be made to be sure that the weight of the mirrors did not influence the vibrations of the middle ear. The best way to do this is to place a similar mirror close

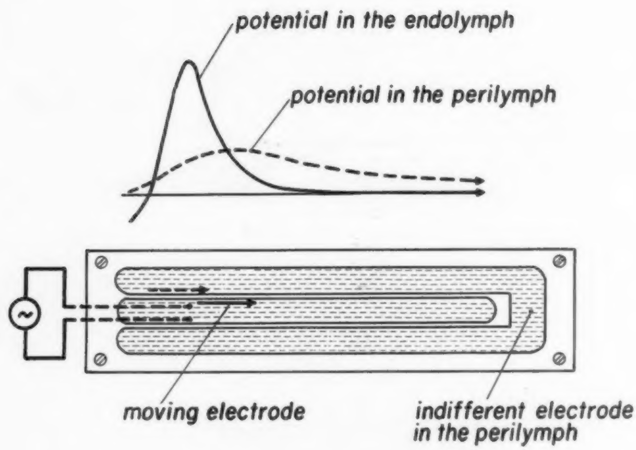

Fig. 3.—A model showing that a local potential produced in one section of the endolymph spreads far out in the perilymph in both directions, if there is electrical insulation between the endolymph and the perilymph. This makes it difficult to make statements about the local potentials from observations made in the perilymph.

to the first one and to decrease the size of both mirrors until no change is observed when the second mirror is glued on.

The free oscillations of the middle ear that were obtained are shown in Fig. 1a. They were very well damped, and much better than in the receivers commonly used. Since that time better receivers are commercially available for measurement purposes (Fig. 1c), but until a few years ago the middle ear was far ahead of communication technique in the quality of the transmission.

These experiments taught me two things. First I realized that it is worthwhile to construct instruments for experiments because they make the results highly reproducible, and make it possible to perform a large series of control experiments without wasting too much time. I guess I spend about two-thirds of my time on control experiments and one-third on the measurements. This gives me a feeling of security. Further, I found that a new technique of ob-

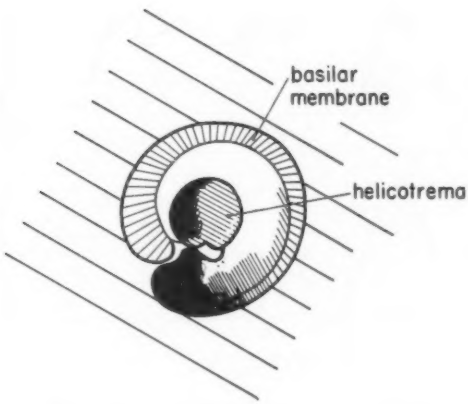

Fig. 4.—If the cupola of the cochlea is ground off, one full turn of the cochlear partition is visible. The opening can easily be closed by a glass plate.

servations is generally followed by a new fact, but on the other hand a new theory may raise many unimportant questions.

Consequently I sought to develop a technique that would enable me to observe the vibration pattern of the cochlear partition.

VIBRATION PATTERN OF THE COCHLEAR PARTITION

At the moment there are two ways to study the vibration pattern of the cochlea. One method is the direct microscopical observation of the vibrations during stimulation of the ear with sound, and the second method is the use of microphonics. Both methods have their advantages and disadvantages, but they supplement each other, and as far as I can see where there is an overlap they lead to the same results. I like to use both methods simultaneously, by observing the vibrations of the cochlear partition with the microscope and recording the microphonics at the same time and place. The high sensitivity of the microphonics permits the investigation of small vibration amplitudes, but only for the larger parts of the cochlear partition. The cochlear partition consists from the electrical point of view of a complex structure of electrical isolating membranes with

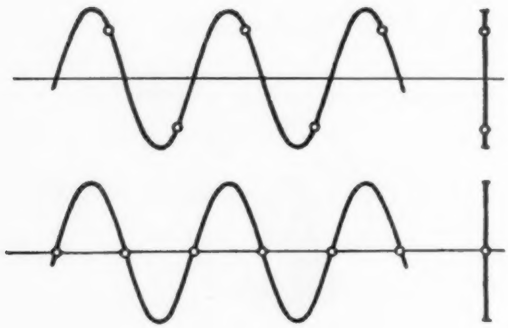

Fig. 5.—One way to measure the phase of an oscillating point is to illuminate it stroboscopically twice during one period. Two light spots are then seen, except when the illumination occurs exactly at the moment the point goes through the equilibrium position. In this case only one point is seen. By adjusting a phase shifter so that this situation occurs, the phase of the oscillating point can be measured relative to another point.

intermediate layers filled with conducting fluids. In such a system any local potential difference can spread far out. To illustrate this we made a plastic model (Fig. 3), consisting of a tube in which a smaller one was inserted, both filled with physiological solution. The physiological solution in the smaller tube should represent the endolymph, and the physiological solution in the larger, the perilymph of the cochlea. The wall of the smaller tube was perforated to simulate the electrical leakage in the Reissner's membrane and the basilar membrane. A moving electrode recorded the potential relative to an indifferent electrode, while on the left side of the model an alternating potential difference was introduced by two electrodes placed in the endolymph. As shown by the solid line in the figure the potentials are quite sharply located in the endolymph near the potential difference which was introduced, but they spread out quite far in the perilymph. If the electrical leakage of the wall of the smaller tube is decreased the electrical potential in the perilymph may flatten out even more. This indicates that the microphonics measured in the perilymph depend on the voltages produced in the organ of Corti and

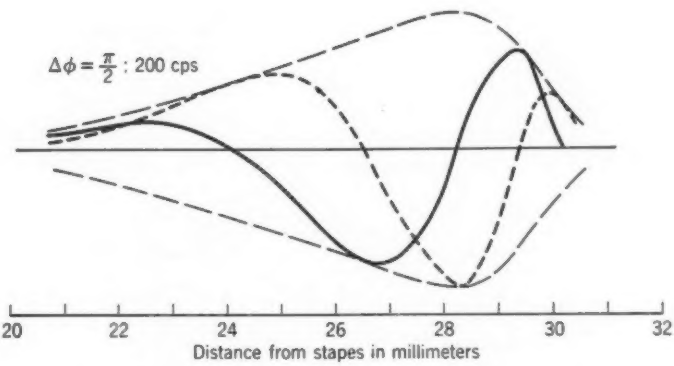

Fig. 6.—Traveling waves measured along a preparation of a human cochlea.

the electrical insulation of the different membranes surrounding the physiological generator. For instance, lack of oxygen can influence both variables in a different way.

On the other hand, direct microscopic observation of the vibrations of the organ of Corti has the disadvantage that, even with an optical magnification of 300 times, the vibrations of the cochlear partition can be seen only at the points of maximal amplitude if the sound pressure used does not exceed the sound pressure at the threshold of feeling. The advantage of the optical method is that observations can be made on different well circumscribed parts such as cells. I made the optical observations on fresh human temporal bones and anesthetized and dead guinea pigs. I did not find any important change in the vibration pattern of the cochlear partition in the first few hours after death.

The observation of the cochlear partition is best done near the helicotrema because there the vibration amplitudes are relatively the largest. It is easy to grind off the tip of the cochlea and thereby expose one full turn of the cochlear partition, as is shown in Fig. 4. The bony part of the cochlear wall can then be replaced with a tight glass plate. For a complete description of the vibration pattern of the cochear partition it is necessary to measure the amplitudes and

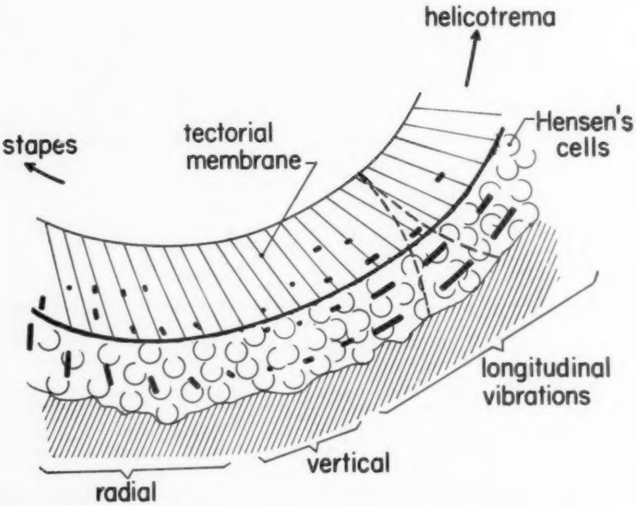

Fig. 7.—Vibrations inside the organ of Corti during stimulation with a pure tone.

the phases of the different parts. With an intense and very fine light beam of a slit lamp it is possible to illuminate corners of some cells so that sharp light spots are seen. When the cochlear partition is set in vibration, these light spots are drawn out to a line, and the length of the line permits the measurement of the local vibration amplitude. It is much more difficult to measure the phase, and a new method had to be developed for this purpose.

In Figure 5 the upper drawing represents the elongations of a particle during the vibrations. If the particle is now illuminated twice for a short time during one period, two bright points can be seen. The distance of these two bright points changes if the phase between the movements of the particle and the time of the light flashes is changed. There is a certain phase angle where the vibrating particle is illuminated precisely at the moment the elongation goes through the central position. In this case only one light point can be seen.

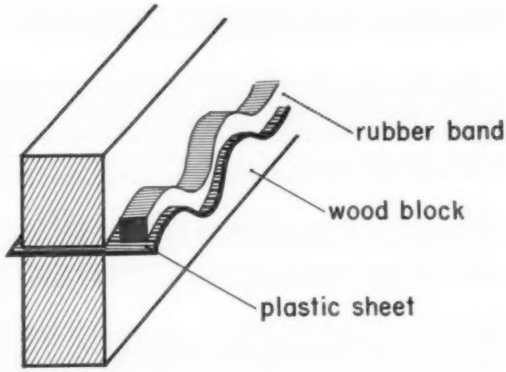

Fig. 8.—Mechanical model to show that the small waves along the basilar membrane are not transmitted to the part of the organ of Corti just below the tectorial membrane.

This coincidence can be very sharply adjusted by a phase shifter. To make the adjustment even sharper I made one flash of the period red and the other green. If they coincide a white point is seen and the eye is very sensitive to the slightest fringe on the illuminated point. In this way it was possible to measure the phase angle between the stapes footplate and the different sections of the cochlear partition during the sinusoidal movements of the stapes, by adjusting the phase shifter so that at the stapes footplate the light spots were white and then measuring the necessary phase change to make the light spots on different parts of the cochlear partition similarly white. Going from the stapes to the helicotrema the phase shifter had to be rotated first slowly and then faster to compensate the phase changes along the cochlear partition. Phase shifts larger than 400 degrees could be obtained. This indicates physically that a traveling wave moves from the stapes footplate toward the helicotrema.

The measurements of this traveling wave for one human temporal bone are presented in Fig. 6. The frequency of the sound was 200 cps, in which case the maximal amplitude of vibration on the cochlear partition is about 28 mm away from the stapes footplate. The dashed line represents the distribution of the amplitude along

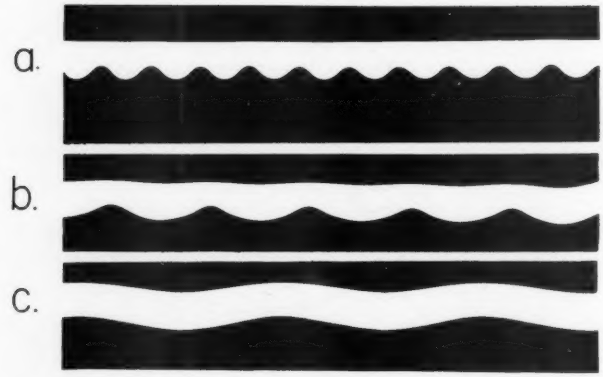

Fig. 9.—If one side of a foam rubber band is deformed according to a sinusoidal line, the other free side of the rubber band does not follow this deformation for short wave-lengths.

the partition. The solid line indicates the position of the partition during the stimulation at a certain instant, and the dotted line the same movement 1.25 millisec. later. The displacement of the wave toward the helicotrema is greater near the stapes than near the helicotrema. If the frequency of the stimulus is increased the whole pattern shifts toward the stapes and the partition in the neighborhood of the helicotrema is left still.

More interesting things that can be seen inside the organ of Corti during vibration are shown in Fig. 7. On the top of the figure is the tectorial membrane, which is relatively stiff and shows only very small movements. Very easy to see with the slit lamp are the Hensen's cells; they look like small fat balls. Further, it can be seen that the whole structure lies on the basilar membrane, which is indicated by narrow cross-hatching in the figure. The interesting thing is that the direction of the vibrations of the organ of Corti changes along the partition, except for the basilar membrane which always vibrates vertical to the plane of the figure. This change in the direction of the vibrations can best be observed in the Hensen's cells. From the stapes to the place of maximal vibration of the basilar membrane, the Hensen's cells vibrate toward the axis of the

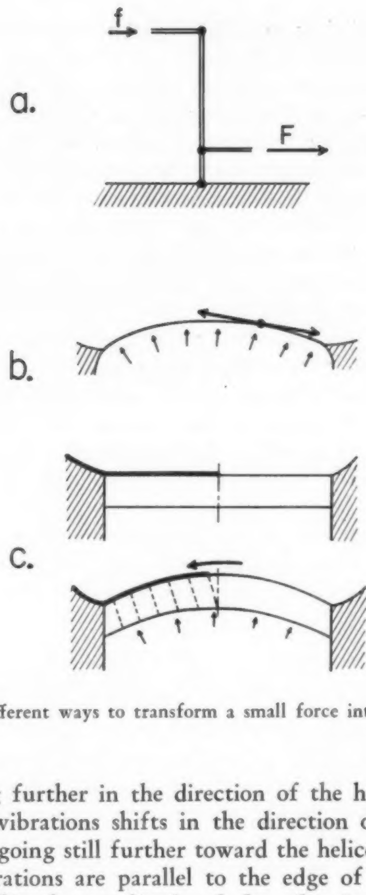

Fig. 10.—Different ways to transform a small force into a large force.

cochlea. Going further in the direction of the helicotrema the direction of the vibrations shifts in the direction of the axis of the cochlea. Then going still further toward the helicotrema for a short section the vibrations are parallel to the edge of the basilar membrane. After this the amplitude of the vibrations decreases below the resolution power of the microscope. At the moment I do not know which of the three sections stimulates or perhaps inhibits the auditory nerves. I worked for three years to develop the stroboscopic slit lamp which permits observation of the cells in the organ of Corti during vibrations, but it will take time to find out which is physiologically the important displacement. In this connection maybe another point is of interest to be discussed.

As seen in Fig. 6 the wave-length of the traveling waves decreases as they approach the helicotrema, and it would be of interest to know how small they get. With the microscope there is no way to observe them because their amplitude is too small. The only way to investigate them seems to be by mathematical analysis. Unfortunately the equations for the movements of the cochlear partition are so complicated that they can only be solved for simplified situations. As the different calculations show, as a consequence of this simplification the wave-lengths of the small waves can be very different. This is particularly true because the measurable data of the cochlear partition are not precise enough to permit a decision on which of the simplifications is correct. To find out further properties of these small waves at the end of the traveling wave a considerable amount of work would be needed. This raises therefore the question of how important these small waves are physiologically. I found in my experiments that small changes in the mechanical properties of the region of the small waves do not change the microphonics even when the electrode is placed in the endolymph. One reason for this may be that the tip of the electrode was still too far away from the place of origin of the microphonics and consequently, as can be seen in Fig. 3, the potentials are flattened out in space and the positive half of the small waves is compensated by the negative half of the same wave at the locus of the electrode. But there may be other reasons too.

The experiments show that the basilar membrane is stiffer than the organ of Corti, because if the organ of Corti is brushed off from the basilar membrane, the traveling waves along the basilar membrane change very little. Therefore we have the picture of a stiff membrane covered with a soft thick elastic sheet (the organ of Corti). If such a combined sheet is bent in long waves the surface of the elastic sheet will follow precisely the wave-form of the stiff membrane. But if the wave-length is short compared with the thickness of the soft sheet, the surface of the soft sheet will not show any deformation. The model in Fig. 8 may illustrate this. A one inch thick, one inch wide band of foam rubber was glued to a one mm thick, four inch wide plastic band. With two specially formed wooden blocks the plastic band could be forced into a wavelike shape. The vertical side of the foam rubber band was photographed and is shown in Fig. 9 for three different wave-lengths. With the short waves practically no deformation of the upper surface can be seen

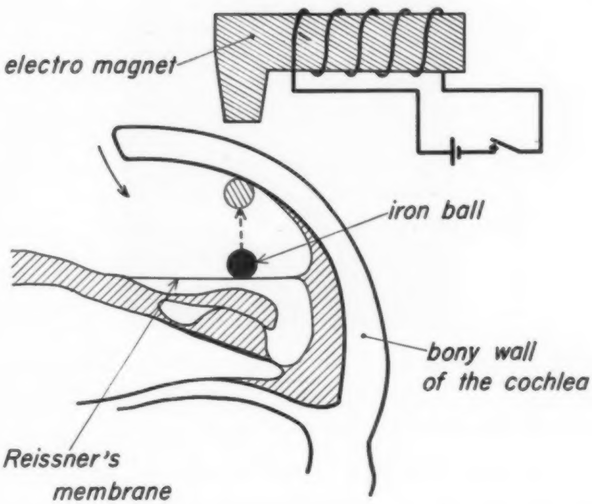

Fig. 11.—A magnetically lifted iron ball was used to give the cochlear partition a short pull.

in spite of the fact that for a wave four to five times longer the surface follows completely the shape of the waves on the plastic band. Therefore if the stimulation of the hearing nerves occurs at a certain height above the basilar membrane, perhaps immediately under the tectorial membrane, the small longitudinal waves of the basilar membrane have very limited physiological importance. This conclusion holds not only for displacements perpendicular to the basilar membrane, but also for displacements in the direction toward the center of the cochlea.

SOME PROBLEMS CONCERNING THE HIGH SENSITIVITY OF THE EAR

One of the most surprising facts in the physiology of hearing is the high sensitivity of the ear. Before the development of amplifiers it was not possible to measure even quite loud sounds because their energy was so small. From this we may conclude that the inner

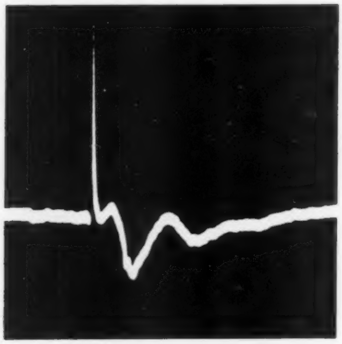

Fig. 12.—A short pull on the cochlear partition produces free oscillations which can be used to measure the energy loss in the cochlea. From such observations it was concluded that the microphonics in the cochlea do not receive their energy from the sound waves.

ear does not waste mechanical energy delivered to the ear drum. The stimulation of the nerves probably results from the deformation of some cells. These cells are solid bodies and therefore their deformation requires larger forces than are necessary to displace fluid particles. Now the question is, how can the pressures in the fluid of the cochlea be increased to such levels that the deformation of the cell bodies will be sufficiently large.

Figure 10 shows the different ways to transform small forces into larger ones. The equipment most commonly used to increase the force is the lever shown in Fig. 10a. A small force *f* can be multiplied several times to a force of *F*. The energy input and output are the same because the force f has to act over a longer distance than force F. A second method is to apply a small air pressure on one side of a membrane. This can produce large tangential tensions in the membrane, as demonstrated in the Drawing B. Another effective system is shown in the Drawing C, where a thick soft membrane is partially covered by a thin inelastic sheet similar to the tectorial membrane covering the organ of Corti. In this case large sheering forces are produced by a relatively small pressure on one side of the thick membrane. I think this is the way the organ of Corti works. The importance of sheering forces in the cochlea has already been

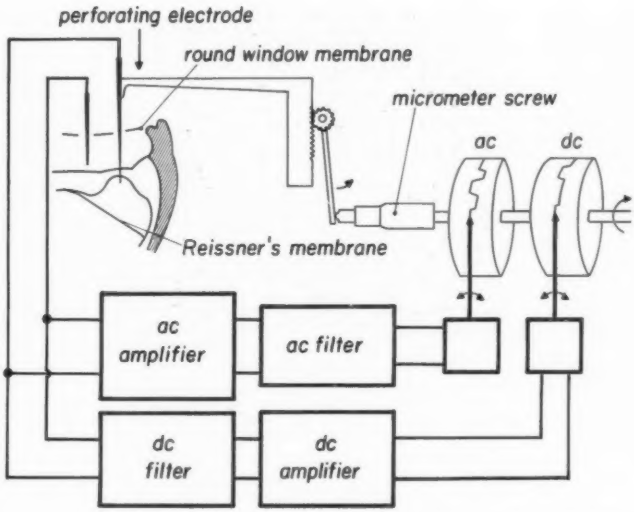

Fig. 13.—Equipment to register the ac and dc potentials inside the cochlear partition by slowly moving a perforating electrode through the different layers.

pointed out by ter Kuile,[1] and their role in the utricle of fish was demonstrated in beautiful experiments by von Holst.[2] This would solve the mechanical problem of optimal force transformation in the cochlea.

Now let us turn to the electrical part of the problem. The production of microphonics looks like a great waste of energy if the incoming mechanical energy in the cochlea is transformed into electrical energy in order to stimulate the nerves. The amount of energy wasted could not be considered a handicap if the incoming mechanical energy is used only to trigger an electric energy reservoir, as in an amplifier. The following experiment was carried out to determine whether the mechanical energy in the cochlea is transformed into electrical energy or whether a trigger action is present. A simple method of measuring the energy loss in a mechanical system is to pull the system and to observe the decrease in the amplitude of the excited vibrations, as was done earlier in Fig. 1. The ratio between

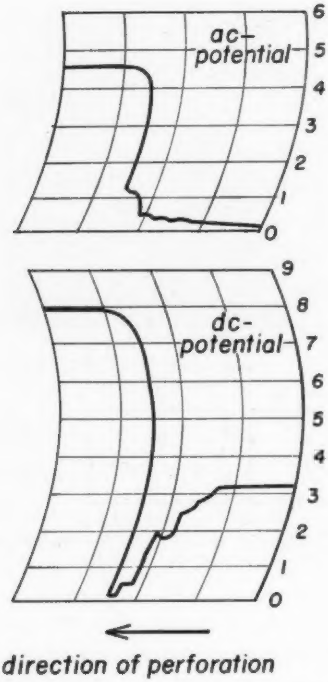

Fig. 14.—Potentials jumps in the organ of Corti during the perforation of the different layers.

two consecutive maximal amplitudes is a measure of the energy loss, or the damping of the system. When an energy transformation occurs in the cochlea, there is a mechanical energy loss produced by the friction of the tissues and the fluid, and a further energy loss produced by the transformation of mechanical energy into electrical energy. Therefore when the electrical energy-transformation is eliminated, the vibrations of the cochlea should be less damped and should last longer. The electric energy loss in the cochlea is due mostly to the microphonics, and they can be reduced by anoxia. If the magnitude of the microphonic voltage is reduced to 1/10, the electrical energy loss will drop to 1/100, so that it can be considered as elim-

Fig. 15.—General set-up for the measurement of the local potentials in the organ of Corti.

inated. From this it follows that the damping of the vibrations of the cochlear partition should change when the size of the microphonics is reduced, and it is correct that the microphonics are produced out of mechanical energy. But if the microphonics are produced by a trigger action, then the damping of the movements of the cochlear partition is only determined by the mechanical friction losses, and they do not change with the introduction of anoxia.

The outline of the experiment is simple, but it was difficult to pull the cochlear partition in the proper way, so that the damping could be measured. In the experiment finally adopted a small iron ball with a diameter of about 1/100 mm was placed on the Reissner's membrane and pulled off by an electro-magnet, as shown in Fig. 11. Figure 12 shows the movement of the cochlear partition produced by the sudden lift of the iron ball. The big spike represents the lift of the ball and the smaller periodic oscillations the free oscillations

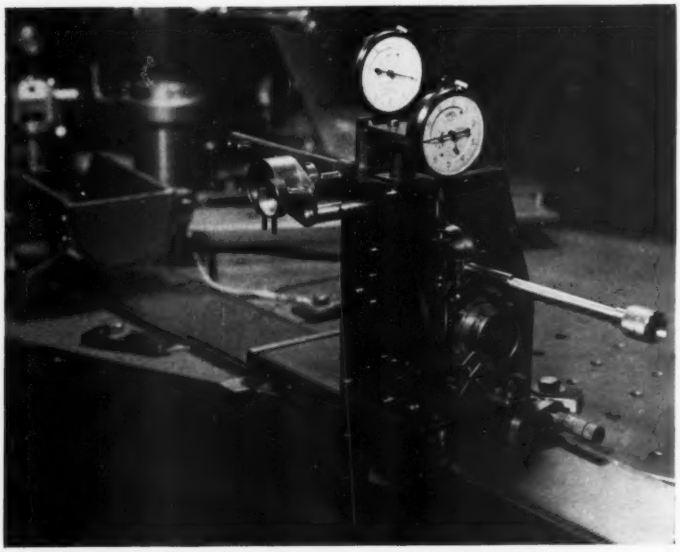

Fig. 16.—Automatic driving unit on which the perforating electrode is fixed.

of the cochlear partition. The movements of the cochlear partition were recorded by the microphonics. Now when anoxia was produced, the sensitivity of the microphonics went down. This was compensated by an increase of the amplifications, but no change occurred in the damping of the free oscillations. Therefore the microphonics must have been produced by a trigger action.

If the microphonics are triggered a large constant pool of electrical energy must be present in the cochlea as long as the animal is alive. Therefore I was looking for large dc potentials inside the cochlear partition that might supply the energy for the microphonics just as the dc batteries in an amplifier supply the energy for the amplified ac currents. It was very easy to find them.

For this purpose, with the equipment shown in Fig. 13, a microelectrode was pushed slowly through the cochlear partition and at

the same time the constant dc resting potentials were recorded with the microphonics produced by a constant sound acting on the stapes footplate. Figure 14 shows the recorded potential difference between the perforating microelectrode and an indifferent electrode obtained in one case. The size of the voltage jumps that occur when one of the membranes is perforated may reach 100 mv. A closer examination of the record shows that there are about three different types of tissues. One is electrically indifferent. Another does not produce microphonics but has large resting dc potentials. The third produces microphonics and at the same time has large dc potentials. The aim of my next experiments will be to correlate the different potentials with the cell structures. This is not easy technically, because the slightest lateral movement of the electrode breaks the tip of the electrode or injures the cells, with the result that the measured potentials of the cells are no longer representative. To minimize accidents, short heavy stands should be used with adjustments specially constructed for the purpose. An over-all view of the equipment I am using now is shown in Fig. 15. The long tube on the left side is the slit lamp which can produce a light beam of 1/100 mm thickness. The microscope has a magnification of about 200 times, and on its left and right sides a pair of electrode holders are located. These holders are mounted on runways that permit their being brought into position in a few seconds with an accuracy of 1/100 mm. In front of the figure the runway for the perforating electrode can be seen, with the thermostat for the animal. Figure 16 shows the holder for the perforating electrode. This holder pushes the electrode completely automatically, according to a predetermined program, through the different parts of the cochlear partition. Once the measurements are started everything runs automatically and the operating table is not touched again. In this way vibrations of the table are avoided.

SUMMARY

This paper summarizes briefly how the vibration pattern of the cochlear partition can be determined, and how the cells in the organ of Corti change their direction of vibration along the partition for different frequencies. It explains why the short waves on the side of the helicotrema, which are so difficult to calculate, are probably not important physiologically.

In the second part attention is called to the sheering forces in the cochlea because the organ of Corti seems to be a kind of mechan-

ical transformer, which transforms small fluid pressures into larger forces on the surface of the cells. Further it is shown that the vibrations in the cochlea trigger electrical ac potentials and a large pool of dc energy is at its disposal for this purpose.

At the end, the measuring equipment used is briefly described.

This research was carried out under Contract N5ori-76 between Harvard University and the U. S. Office of Naval Research, U. S. Navy (Project NR 142-201, Report PNR-149). Reproduction for any purpose of the U. S. Government is permitted.

HARVARD UNIVERSITY, MEMORIAL HALL.

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XXXVIII

THE EXCITATION OF NERVE IMPULSES IN THE COCHLEA

Hallowell Davis, M.D.

St. Louis, Mo.

There are too many new experimental observations on the electrical and neural activity of the cochlea to attempt a complete review in the time available. We will therefore center attention on two points: first a generalization as to the distribution of excitation along the cochlea, and then a brief description of the electrical potentials in the cochlea, their anatomical location and their probable relation to the excitation of the nerve impulses.

The generalization, which is closely related to Professor Békésy's description of the mechanical events in the cochlea, is that low frequencies not only cause mechanical movement of the cochlear partition of the basal turn but also excite nerve impulses in the nerve fibers that serve it. The place theory of cochlear analysis of sound is to be interpreted, not as meaning that a given frequency excites only a given restricted area but rather that frequencies differ chiefly in the extent of the partition that they excite. If there is an optimum region of greatest excitation the "peak" is very flat. The sharpness of the localization is to be found not in a sharp peak of activity but in a sharp boundary between an excited region and the unexcited region beyond this boundary. The excited region begins near the oval window, even for low tones.

This unsymmetrical extension of the excited area to one side only of the "place" that is correlated with frequency is reflected in the unsymmertical masking of high tones by low but not of low tones by high. Now we know that the asymmetry begins in the cochlea and is here greater if anything than it is in the masking functions. The electrical evidence for these statements rests on three types of experiment, one on the cochlear microphonic, another on the

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This work was supported by a contract between the Office of Naval Research and the Central Institute for the Deaf.

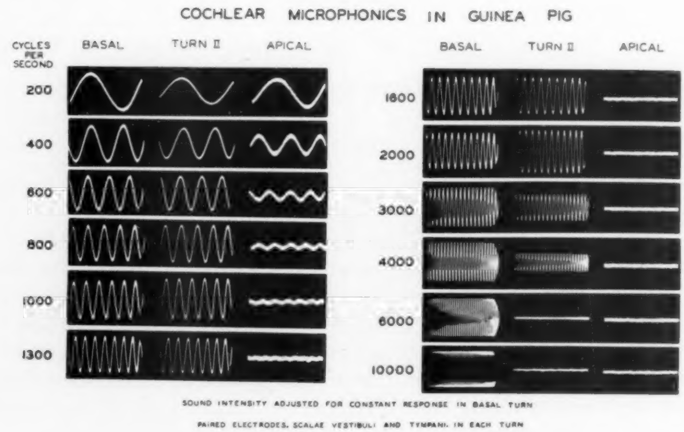

Fig. 1.—Simultaneous oscillograms from Turns I, II, and IV. The amplifications of three channels were initially adjusted to give approximately equal responses in all three turns at low frequencies. As the frequency was changed the sound-pressure level was adjusted to maintain a constant response (200 μV, peak-to-peak) from the basal turn (left column).[13]

nerve impulses in the auditory nerve and the third on the nerve impulses in the cochlear nucleus.

Differential electrodes, one in scala vestibuli and the other in scala tympani of the same turn, allow us to record the cochlear microphonic from short segments of the cochlear partition—segments that are effectively only about 2 mm in length. The details of the evidence for this statement have been presented elsewhere.[13] The nature of the resulting "sound analysis" in the cochlea is illustrated in Figures 1 and 2. Also we can poison the apical region with KCl without affecting the response to low tones from the first turn.[14]

The CM is probably the mechanism by which the nerve impulses are excited. Even if it is not we may take it as one index of excitatory effect because it seems to be proportional, within limits, to the displacement of the basilar membrane. Now we obtain from the basal turn cochlear microphonics that are of the same order of magnitude for a given sound pressure for low tones as for high (± 10

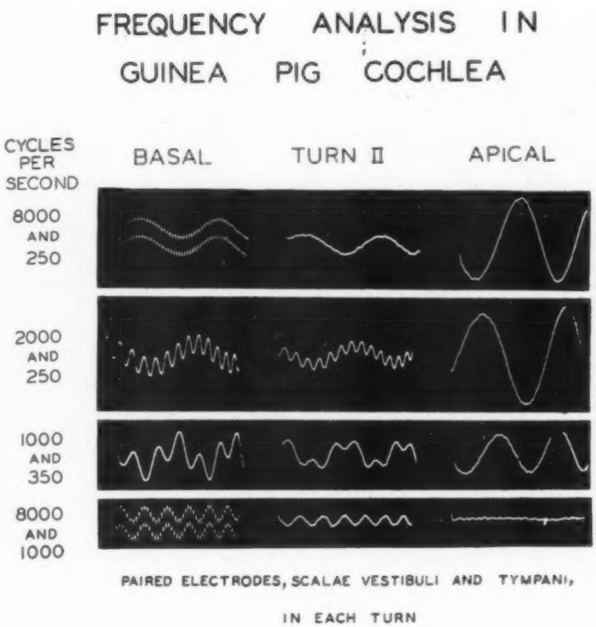

Fig. 2.—Same as Fig. 1 except that the amplifications are the same in all three channels. The intensities of the two tones, at the frequencies indicated at the left, were adjusted to give equal responses (160 μV, peak-to-peak) in the basal turn. The corresponding response from Turn IV was exceptionally large in this experiment (680 μV).[13]

db from 100 to 8000 cps). The details of this relationship are still being worked out by my colleagues, Drs. Eldredge and Benson, but from the general picture we predicted that a nerve fiber which can be excited by high-frequency tones and therefore comes from the basal turn should also be excited rather efficiently by low frequencies. The experimental test of this assumption was made successfully by Tasaki.[10] He approached the auditory nerve of the guinea pig by drilling a hole through the bone from the bulla (Fig. 3). He inserted extremely fine pipette electrodes, less than a micron in diameter at the tip, which entered individual nerve fibers. The technique is

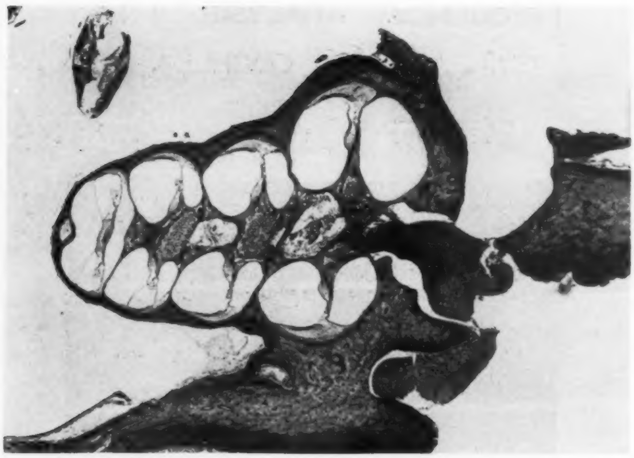

Fig. 3.—This mid-modiolar section of a guinea-pig cochlea shows a hole drilled inward from the bulla through which microelectrodes were introduced into the medulla or the auditory nerve. Note the division between the lighter cell-rich area of brain and the darker auditory nerve.[10]

difficult and the electrodes, in spite of their very small size, injured the nerve fibers and they soon ceased to conduct impulses. But some fibers were studied long enough to verify our predictions.

The stimuli that were employed were very brief bursts of tone that were systematically and rapidly varied in frequency. The sound level was changed systematically and it is evident from the accompanying slide that fibers which were excited by fairly high frequencies in the neighborhood of 8000 cps also responded to tones of very much lower frequency at only slightly greater intensities (Fig. 4).

Figure 5 shows that the nerve impulses are excited in only one phase of the stimulating tone. It is not always at exactly the same phase to be sure, but for a given fiber it is always in the same half cycle of the sound wave. Figure 5 shows the responses from two different fibers. You will see that one of the fibers responds in the rising phase, the other in the falling phase, of the cochlear microphonic of the basal turn. This relationship at first glance seems to

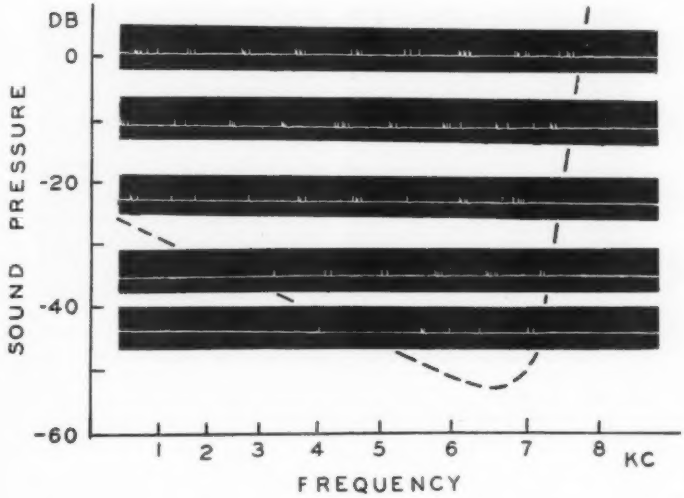

Fig. 4.—This single auditory nerve fiber responded to tone pips of many different frequencies and intensities. The dotted line shows the boundary of its response area. The reference level (0 db) of intensity is arbitrary.[10]

contradict the assumption that the cochlear microphonic is the direct stimulus to the nerve fiber, because if it is we should expect that at such a low frequency (500 cps) the nerve impulses would always be excited in more or less the same phase of the exciting electric current. But we now know very well that different parts of the basilar membrane move out of phase with one another except for the very lowest frequencies.[13] We believe that in the experiment of Figure 5 one of the nerve fibers came from the basal turn and the other from a much more apical region where the membrane was lagging in its movements by approximately half a cycle. In other words we take the difference in phase as evidence that one of these fibers came from the basal turn—yet it was excited successfully by the 500 cps tone. Incidentally this experiment also shows that the nerve impulses in response to low tones are not all of them grouped into the neat synchronous volleys that are emphasized by the so-called volley theory of hearing. The volley principle is correct, of course, as has been

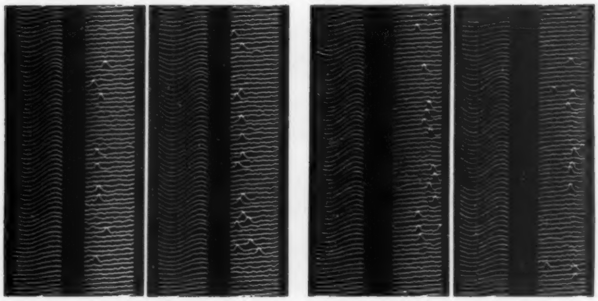

Fig. 5.—The responses from two different single fibers in the auditory nerve (right columns) show different phase relations to the cochlear microphonic. The latter (left columns) was recorded simultaneously from the basal turn by differential electrodes. The stimuli were brief bursts of 500 cps tone at about 40 db above human threshold. These are continuous recordings, to be read from bottom upward and from left to right.[10]

demonstrated experimentally, but it is correct only in a broad statistical sense. The impulses in some fibers lag systematically behind those in other fibers.

Dr. Tasaki[11] has also explored once more the cochlear nucleus where Galambos and Davis[8] first recorded the activity of individual auditory units more than ten years ago. Tasaki used the same operative approach (in the guinea pig) that he used for the auditory nerve but he directed his electrodes more deeply into the medulla into what was probably the dorsal cochlear nucleus. Here he could record unitary responses and fortunately these units survived rather better than those in the auditory nerve. From the latency of the responses he could be quite sure that some of the units were separated from the primary neuron of the auditory nerve by at least one synapse. The sensitivity of two of these units to tones of systematically varying frequency is shown in Figure 6. The pattern is substantially the same as for the primary neurons. There is a sharp upper limit to the frequency band that will stimulate. Lower frequencies, even very much lower frequencies, excite these same units almost as efficiently. This figure illustrates particularly well the unsymmetrical relationship to the frequency of the stimulating tone. We do not

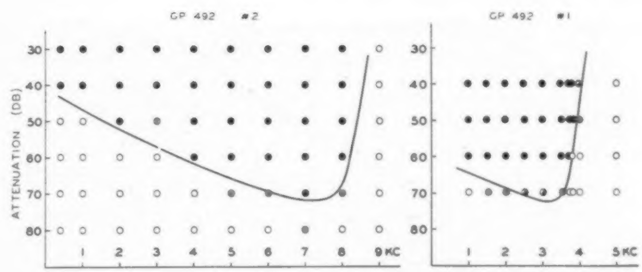

Fig. 6.—Response areas of two elements in the cochlear nucleus. Solid dots = clear strong response; half-filled circle = weak but recognizable; cross in a circle = doubtful; empty circle = none. Abscissa is frequency of pure-tone stimulus in kilocycles. Ordinate is attenuation in decibels from an arbitrary high level.[11]

yet understand how the sharper response areas that were found by Galambos and Davis are brought about, but we strongly suspect that the process of inhibition[9] is responsible for the "sharpening up" of the response of the Galambos-Davis elements. It is possible that the different time relations of impulses in different fibers, which was illustrated in an earlier figure, enters into this process in some way, but we will speculate no further in this direction at the present time.

Let us turn back now to the cochlea itself and the possible mechanism of excitation of nerve impulses. By this time we should all be familiar with the fact, first reported by Békésy,[1] that the endolymph in the scala media is electrically positive relative to the perilymph and surrounding tissues by as much as 50 to 100 mV. This observation we have repeatedly confirmed in our own laboratory and we have confirmed also the existence of a negative potential in the area adjacent to the basilar membrane where the hair cells, the cells of Hensen and the cells of Claudius are located. Békésy has also described a negative potential in the cells of Reissner's membrane and of the stria vascularis. Such negative potentials are easy to understand. They are similar to the negative potentials found inside of axons of nerve fibers, in muscle fibers and probably inside of all or nearly all living cells. It is the positive potential of the scala media which is surprising, both because of its magnitude and because of its

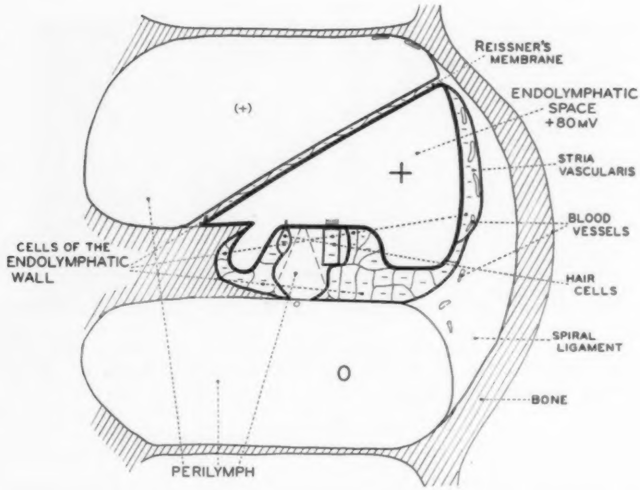

Fig. 7.—Interpretive diagram of the endolymphatic space and the distribution of DC potentials within the cochlea. The heavy line represents the boundary of the endolymphatic space. The potential within it is uniform and strongly positive relative to scala tympani. The walls of the endolymphatic space are composed of cells. Within these cells, while uninjured, the potential probably averages about –40 mV relative to scala tympani. Our measurements run as high as –60 mV in the organ of Corti. For Reissner's membrane Békésy[1] says "–20 mV and may have been even higher." The degree and distribution of the negativity in stria vascularis is still very uncertain. The negative intracellular potential rapidly decays or is lost if the cell is seriously injured by the exploring electrode. The tectorial membrane seems to be electrically "transparent," like the spiral ligament, and is omitted in this diagram. Only one external hair cell is shown. The reasons for indicating perilymph in the tunnel of Corti are given in the text.[12]

positive polarity. This DC potential is sensitive to lack of oxygen and fails very nearly in parallel with the cochlear microphonic. Apparently the DC potential is actively sustained by the metabolism of some group of cells that lies in the wall of the endolymphatic space. The anatomical boundary of the positive potential is illustrated in Figure 7. It is the surface of stria vascularis, of Reissner's membrane, of the cells of Claudius and Hensen, and the reticular lamina that is in contact with endolymph. Here must be a wall across which ions

cannot pass freely, for otherwise the high DC potential would be dissipated rapidly. It is the area of the endolymph that is positive. We will summarize some of our recent studies[12] of this endolymphatic potential without going into experimental details.

First, the electrical potential of the scala media is increased, that is, is made more positive relative to the perilymph, by increase of hydrostatic pressure either in the scala vestibuli or the scala media. It is reduced by increase of pressure on the side of the scala tympani. It seems reasonable to suppose that it is the displacement of the basilar membrane, or more probably the resulting displacement of the tectorial membrane relative to the basilar membrane, that is responsible for these changes.

Second, the cochlear microphonic seems to be closely related to the DC potential. If the latter is increased by adding an electrical polarizing current in the proper direction the cochlear microphonic is increased and if the endolymphatic potential is reduced by reversed polarization the cochlear microphonic is proportionately reduced. We have already mentioned the similar behavior of the DC potential and the cochlear microphonic when the oxygen supply is cut off.

Third, the DC potential and the cochlear microphonic do not always go hand in hand. If we replace the perilymph in the scala tympani with Ringer's solution that has been enriched by the addition of potassium, which incidentally would make it much more like endolymph as Dr. Catherine Smith has shown, the DC potential is not affected. The cochlear microphonic is abolished by this procedure and so are the nerve impulses. We conclude from this not only that it is possible to dissociate the cochlear microphonic from the DC potential but also that the basilar membrane is permeable to potassium.

Fourth, the anatomical source of the cochlear microphonic now seems to be established beyond question as the hair-bearing end of the hair cells.[12] It seems, therefore, that the potassium introduced into the scala tympani poisons the mechanism which produces the cochlear microphonic. But potassium-rich Ringer's solution introduced into the scala vestibuli has no effect on the cochlear microphonic. This is not surprising, as we have already concluded that Reissner's membrane must be impermeable to ions and furthermore we know that the endolymph is already much richer in potassium than the fluid that we introduce into the scala vestibuli.

A corollary of these conclusions is that the tunnel of Corti, the space of Nuel and the other spaces within the organ of Corti are not filled with endolymph but are filled with perilymph. The impermeable barrier, we repeat, is not the basilar membrane but the reticular lamina. This suggests incidentally that the nutrition of the organ of Corti, including the hair cells, is derived from the scala tympani and not from the scala media. This point is so far merely an inference and not directly proven but it nevertheless seems highly probable. Incidentally, if the tunnel of Corti were filled with fluid of the chemical composition of endolymph the nerve fibers which are immersed in it would not be able to conduct nerve impulses.

About two years ago I described a model for the excitation of nerve impulses in the cochlea.[2-4] According to this suggestion the stria vascularis is the source which maintains the positive DC potential of the endolymph. The hair-bearing ends of the hair cells are assumed to act as variable resistances which allow more or less current to leak through, and this resistance is supposed to vary according to the traction or bending exerted by the tectorial membrane on the hairs. The resulting alternating current component of the leakage through the hair cells is supposed to traverse the nerve fibers and thus excite the nerve impulses.

At the time I proposed this model it sufficed to explain all of the known facts concerning the DC potential, the cochlear microphonic, and the excitation of the nerve fibers. Now I must report that the model is no longer adequate. Dr. Tasaki, Dr. Eldredge and I[12] have explored the area of the spiral ligament close to the stria vascularis and also the tympanic surface of the basilar membrane for evidence of current flow such as was required in the model to complete the circuit back from the tunnel of Corti to the "battery" in the stria vascularis. We were unable to find evidence of adequate current flow sufficient to account for the rather large changes in DC potential that can be produced by hydrostatic pressure in the scala vestibuli or the scala media. Possibly the return circuit exists but is hidden in the blood stream. A simpler explanation is to assume that the DC is generated in the hair cells and is directly modulated in some way that we do not understand by the deformation of the hairs at the upper end of the cells.

We have also added many other puzzling facts, and for the present it seems more profitable to continue to add new facts and

verify old ones than to try to modify the model or construct a new one every two or three months to keep up to date. It seems highly probable that the cochlear microphonic is closely related to the DC potential, but we do not know the physical or rather the biochemical mechanisms underlying either of them. I believe that the cochlear microphonic is the immediate stimulus to the nerve impulses, but the issue is confused by the presence of a fourth potential, the "summating potential," which we described three years ago.[6] We later suggested that the summating potential is nothing but the neural activity of the terminations of the auditory nerve in the organ of Corti,[7] but some of our present experiments, still unreported, are leading us to doubt the adequacy of this explanation.

In the midst of the present welter of new facts about the mechanics and particularly about the electrophysiology of the cochlea we can only say that the entire situation is obviously very complicated indeed! My final conclusion therefore is that we must expect that an explanation that will include all of the new facts must be complicated. For a time it was legitimate to take a simple-minded point of view towards the problem of excitation of nerve impulses in the cochlea, but such simplicity of thinking has now ceased to be a virtue.

We are indebted to the Journal of the Acoustical Society and to the Journal of Neurophysiology for permission to reproduce Figures 1, 2, 7 and Figures 3, 4, 5, and 6 respectively.

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XXXIX

POSITIONAL NYSTAGMUS

Terence Cawthorne, F.R.C.S.

London, England

When your President honoured me with an invitation to read a short paper at this meeting I at once thought of positional nystagmus.

I did so because at the National Hospital for Nervous Diseases, Queen Square, London, we get a steady flow of these tricky cases through our clinics, and I have the impression that they are on the increase.

Our growing appreciation of positional nystagmus is in no small measure due to the fact that our attention has been repeatedly drawn to this subject by the writings of Nylen[9] of Uppsala and of your Secretary, Dr. John Lindsay,[7] both of whom have made outstanding contributions to the study of this intriguing condition. My colleagues at the National Hospital, Dr. Hallpike and Dr. Dix,[3] have also recently added a great deal to our knowledge of positional nystagmus and I am glad to have this opportunity of confirming their findings.

In my clinics every patient in whom a lesion of the vestibular system is suspected is examined for spontaneous nystagmus, also for positional, and finally for optokinetic nystagmus. In addition, of course, nystagmus induced by caloric stimulation is noted and also sometimes that following rotatory stimulation. In fact I would go so far as to say that the examination of the vestibular apparatus is incomplete if the test for positional nystagmus is omitted.

It is not easy to put into words an exact definition of positional nystagmus and it may help to start off by mentioning the way in which we test for spontaneous nystagmus. The head is held in the normal erect position and the eyes are examined for any movements with the gaze directed straight ahead, then to one side (but not beyond the limits of binocular vision), then to the other side and finally up and down. In testing for positional nystagmus the gaze is held

straight ahead and any nystagmic movements which are induced by altering the position of the head from normal erect posture are included under this heading. In practice this means lying supine with the head back or turned to one or other side. We have found that to test with the head in any other positions adds to the duration and difficulty of the test without seeming to give any additional information.

There is usually a sensation of vertigo accompanying the nystagmus, which is often severe and startling; though occasionally it may be slight. We have had no experience of patients who have positional nystagmus without any vertigo at all.

Most observers have regarded positional nystagmus as a sign of a disturbance of the vestibular system either in the end organ or in its central connections. This point was particularly stressed by Lindsay[7] in his paper before this Society in 1951. If peripheral, as first suggested by Barany,[1] it is most likely to be in the otolith apparatus of the static labyrinth. If central, then, as shown by Nylen and others, the vestibular centres in the cerebellum are the most likely site of the lesion.

Now although vertigo and nystagmus are the most striking features of a disordered labyrinth, I have found that two-thirds of the positional group do not exhibit any other signs of labyrinthine disease at all and only a few have signs of disturbance within the central nervous system.

This does not, however, exclude the labyrinth as a probable source of the complaint. We already know that it is possible to have a vestibular disturbance without any impairment of cochlear function. Dix and Hallpike have shown that there can be a lesion of the static labyrinth with a normal response to caloric stimulation. For this reason we must regard the testing for positional nystagmus as part of the routine examination of vestibular function.

The main obstacle to a better undertsanding of the pathology of non-suppurative disorders of the labyrinth has always been the benign course they follow, so that the opportunity for detailed histological examination of the labyrinth rarely arises, and this applies particularly to positional nystagmus.

Once again we have reason to be grateful to my friend and colleague Hallpike for he has followed up his discovery with the late

Sir Hugh Cairns[5] of labyrinthine hydrops, with the recent demonstration with Dr. Dix of a lesion of the macula utriculi in a case of paroxysmal positional vertigo of the peripheral type.

Dix and Hallpike also describe their experience with a series of similar cases all of which they believe are due to a lesion within the labyrinth, often the result of some infective or traumatising agent. Working at the same hospital, though for the most part with different patients, I have had similar experiences.

Though as yet there is only the histological evidence of one case to go on, the clinical picture presented by a large proportion of the cases in both series is so strikingly similar as to leave but little doubt that in such cases it is the result of a disorder located in the static part of the vestibular labyrinth.

THE TEST

To test for positional nystagmus the patient is first of all seated on a couch. Then he is told that he is going to be laid back on the couch with the head turned first to one side, then to the other, and finally straight back. He is warned that in one or other of these positions it is possible that he will feel giddy, but that it will not last for long, and no matter what he feels it is imperative that he should keep his eyes open all the time and look straight ahead. Then holding the patient's head between his hands the examiner lays him back on the couch in the supine position with the head to one side. This movement should not occupy more than three seconds. If there is no nystagmus after ten seconds the patient is brought upright the examiner still looking for any nystagmus. After a further ten seconds the patient is again taken back into the supine position this time with the head to the other side. Again if there is no nystagmus after ten seconds in this new position, the patient is brought upright, observed for any nystagmus and then taken back again, this time with the head straight back, but not hanging too far back. Thus the test is done with the head in three different positions and the whole test if negative will not, as you will see in the film, occupy more than one minute. If positive in one or more head positions, it will not take longer than three minutes. Thus the test is easily and quickly carried out and does not call for any special equipment.

If, however, in any of these positions of the head nystagmus appears, any latent period between adopting the position and the

onset of the nystagmus is carefully noted. Further, the direction, intensity, and duration of the eye movements are also noted. If the nystagmus is sustained unabated for thirty seconds it is likely to remain so long as the critical position is held.

It has not been found necessary regularly to make the test with the head in any other position and we have found that these nystagmic reactions appear just the same when the whole body is turned to one side in such a way as to avoid turning the head on the neck. Thus turning the head only in no way modifies the result and it is a much simpler procedure than turning the whole body.

If in one or more of these positions of the head nystagmus appears, then the position is held for thirty seconds after which the patient is brought upright, and then after a short pause the same position is renewed. If the nystagmus does not reappear then it is described as being readily fatiguable; if it reappears with diminishing intensity, and at further attempts does not appear at all, it is described as gradually fatiguable. If on the other hand it continues with undiminished intensity despite repetition, it is considered nonfatiguable.

As the result of carrying out the test for positional nystagmus in this way, it has been possible to separate the cases into two groups, based on the behaviour of the nystagmus. Furthermore we have found that one of these groups includes all the patients who have a lesion in the central part of the vestibular system, while in the other group are found those with a peripheral lesion in the end organ. In one group, the nystagmus appears as soon as the head arrives in the critical position, and it continues to beat at a steady rate for so long as the head is held in that position. It will also start to beat again every time that position is resumed. Frequently it appears in more than one position of the head and the direction of the nystagmus may change with the direction of the head. This group in which the nystagmus is steady and nonfatiguable includes all the patients with a proven lesion of the central vestibular connections, and also two others in whom a central lesion is considered likely, but which as yet has not been verified. Often but not invariably the associated vertigo is slight. We call this the central type of postional nystagmus and it has been seen in just over 10 per cent of the cases in this series.

TABLE 1.
POSITIONAL NYSTAGMUS.

PERIPHERAL (static labyrinth)	114
CENTRAL (mid-line cerebellar)	13

In the other and much larger group there is a latent period of from two to ten seconds between taking up the critical postion and the onset of the nystagmus. The eye movement can be tumultuous, often with a wide excursion, and is usually a combination of rotatory and horizontal movements, though I have sometimes observed it to be vertical or even oblique. This dies down in from five to thirty seconds. After bringing the patient upright there may be a return of the eye movement and vertigo in an opposite direction for a few seconds, and then on resuming the same supine position the nystagmus will either not reappear or only come on with diminished intensity, finally to disappear on the third or very occasionally fourth attempt. After this it cannot be made to reappear for from several minutes up to half an hour. In this group there is a real paroxysm of nystagmus (and of course vertigo) which appears as a rule only with the head in one position and which is fatiguable. Barany was the first to describe this fatiguability and I was interested to find in a discussion of Dr. Lindsay's paper given before this Society in 1951 that Dr. Robert Hunter had also observed it. All the patients who had additional signs of a peripheral vestibular lesion came within this group, and, as Hallpike and Dix have shown, even those without any other sign of a vestibular lesion but who behave in this manner probably have a utricular or saccular lesion. This paroxysmal and fatiguable nystagmus is the peripheral type. It has accounted for nearly 90 per cent of my series, and of these not more than a third yielded additional evidence of a labyrinthine lesion.

So far in my experience it has been possible to put every case into either the central or the peripheral group, but there are one or two other features which are of interest and which may help to localize the lesion more precisely.

Position of the Head. In most of the central group the nystagmus appears in more than one of the head positions, and the eye movements may or may not change direction with the position of the head. This would correspond with the Type I or direction changing of Nylen and Lindsay. In the peripheral group the nystagmus is often only seen with the head in one position almost always with the affected labyrinth undermost. This is the Type 2 or direction fixed of Nylen and Lindsay, and others. I have however, two patients with paroxysmal and fatiguable nystagmus occurring with head both to the left and to the right and in both of these there was additional evidence that both vestibular labyrinths were affected. At first sight these cases might be taken for Group I, but further consideration reveals that the nystagmus in each case was both limited and fatiguable, and not continuous and non-fatiguable as in the real central type, and that really these were direction fixed with both labyrinths affected. This suggests that a distinction between central and peripheral positional nystagmus along the lines already indicated is to be preferred because it is both simple and we believe accurate.

POSITIONAL VERTIGO

Positional vertigo in the central group is rarely severe, though some dizziness has been present in every patient I have examined. It is possible that a routine examination of all cerebral tumours would reveal that a proportion of them would exhibit positional nystagmus without vertigo, though my friend Dr. Edwards tells me that he has tested a number of patients with tumours of the posterior fossa but without vertigo and in none was he able to elicit positional nystagmus. We do not however have the head hanging right back to its fullest extent and it may well be that just as in testing for spontaneous nystagmus we restrict the deviation of gaze thus avoiding the eye movements which often occur in the extreme position, so in this test avoidance of over extension of the head limits the number of cases in which eye movements might be seen. In two cases in the central group, however, in neither of which the lesion has yet been verified, the vertigo was terrifying in its intensity and to make things worse it was accompanied by vomiting. My neurological colleague at the National Hospital, Dr. E. A. Carmichael,[2] thinks that in these two cases there may be a small vascular tumour in the midline in the cerebellum. In the peripheral group the vertigo was on the whole much more severe than in the central group. In some

TABLE 2.
POSITIONAL NYSTAGMUS
SIGNIFICANT HEAD POSITION.

	1. Head back only	2. Head back and to one side	1 & 2
PERIPHERAL:	7%	85%	8%
CENTRAL:		38%	62%

patients the thought of the vertigo coming on was so distasteful that it took some persuasion to make them take part in the test. In the more dramatic cases the onset of the vertigo would be heralded by a cry of alarm from the patient who might even clutch hold of the examiner for support. There is a small group of patients in whom there is a positional vertigo with latent period and fatiguability, without however any nystagmus. In some instances the nystagmus disappears before the vertigo.

Injury. In the peripheral group some form of head injury seems to have been the commonest etiological factor. The injury does not have to be severe, and in fact I have found that several cases have followed a general shaking by jumping down onto their heels. This connection between head injury and positional vertigo has been noted by other observers including Barany, Dix and Hallpike and also Dr. Robert Hunter.

Infection. As in certain other unusual forms of vertigo of vestibular origin such as vestibular neuronitis, infection either in the shape of former local infection or of focal sepsis, seems to play a definite part too in the causation of peripheral positional vertigo. In this connection I would like to pay a tribute to the memory of my friend A. J. Wright[9] of Bristol. He was a great champion of the importance of focal sepsis in the etiology of aural vertigo, and although Hallpike and I used not to see eye to eye with him about the role of focal sepsis in the causation of Ménière's disease, we have

TABLE 3.
POSITIONAL NYSTAGMUS
ETIOLOGY OF PERIPHERAL GROUP.

Head Injury	34
Infection	24
Unknown	56

TABLE 4.
POSITIONAL NYSTAGMUS
SEX INCIDENCE.

	PERIPHERAL	CENTRAL
Male	44	10
Female	70	3

no doubt that it has a place in the causation of some of these other vestibular disorders which have been given, though I doubt whether they deserve it, the sobriquet of pseudo-Ménière's disease. Table 3 shows the frequency with which there was a definite history of injury or infection in this series.

The preponderance of females over males in the peripheral group (Table 4) may in part be accounted for by the fact that those who have to do a lot of stooping down and stretching up in their everyday life will find this positional nystagmus much more of a nuisance than those who are able to keep on an even keel. Housewives for instance find this condition very troublesome as do men involved in the maintenance of automobiles.

This is a disease of early to middle life though the earlier age at onset in the central group is probably accounted for by the relatively high incidence of posterior fossa tumours in the young.

OTHER SIGNS OF VESTIBULAR DISTURBANCE

As Table 6 shows, in the peripheral group the caloric test was abnormal in less than one third of the cases and surprisingly enough it was more frequently abnormal in the central group. Some hear-

TABLE 5.
POSITIONAL NYSTAGMUS
AGE INCIDENCE.

	PERIPHERAL	CENTRAL
Under 50	63	10
Over 50	51	3

TABLE 6.
POSITIONAL NYSTAGMUS
CALORIC ABNORMALITY.

Peripheral	31%	(35)
Central	62%	(8)

ing loss was present in 28%, but in only 8% did there seem to be any connection between the deafness and the positional nystagmus.

In the peripheral group it was interesting to find that in nearly one-third there were periods of remission lasting for days or weeks, during which the nystagmus could not be induced to appear. In this respect positional nystagmus behaves like labyrinthine hydrops, though there is nothing else to suggest that they have anything in common.

In many cases it is a self-limiting disease and certainly in all the peripheral group it is benign.

As we are becoming more familiar with this condition we find that a careful history affords valuable clues to the true state of affairs. In well over half of the peripheral group, the main complaint was of vertigo coming on during the resting hours. Either it could be induced in bed when turning over or when just lying down, or when getting up in the morning. In a few it was originally noticed in the bathroom when washing the face or when throwing the head back for shaving.

Whatever the cause it is important that we should learn to distinguish between the central and peripheral groups. Testing for positional nystagmus should form part of the routine examination of

the vestibular apparatus and I regard it as a simple but effective way of enquiring into the integrity of the static labyrinth.

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XL

MÉNIÈRE'S DISEASE: SIMPLIFIED SURGICAL MANAGEMENT

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In the surgical management of Ménière's disease many operations and procedures have been recorded through the years. The most prominent among these procedures was that emphasized by McKenzie[1] and Dandy[2] who advocated a suboccipital approach to the vestibular portion of the eighth nerve. This operation was a major affair in which the occipital lobe was exposed and the subarachnoid space opened. The eighth nerve was exposed and its vestibular portion was sectioned. This procedure did not prove to be wholly satisfactory, as in some cases not sufficient of the labyrinth filaments were sectioned and if the section extended into the auditory portion there was a loss of hearing which tended to occur anyway in many of the cases as the years passed. Complications and undesirable side effects were not uncommon.

This procedure was not warranted in many of the cases operated upon as there was not sufficient hearing present to justify an operation of this extent with a hope of saving the little unworkable hearing which remained.

Richard Lake[3] was first to operate on the labyrinth for vertigo. In the year 1904 he removed the entire horizontal semicircular canal in a case of unilateral aural vertigo with complete relief of vertigo.

Putnam[4] exposed the superior semicircular canal by way of a subtemporal decompression and passed an electric current through an opening in this canal into the vestibule with relief of dizziness. Wright[5] approached the labyrinth by making an alcohol injection through the tympanum and oval window and reported his results in 60 cases. Cawthorne[6] removed a section of the vestibular membrane through an opening in the horizontal canal. This removal of a section of the membrane, however, was not necessary since any wide injury to the vestibular labyrinth in the region of the ampulla will

cause the entire cochlear and vestibular portion of the eighth nerve to die. Day[7] approached the labyrinth directly with an opening in the anterior portion of the horizontal canal and ampulla, followed by the use of an electric cautery to the utricle in the hope that the vestibular function might be destroyed and at the same time save the organ of hearing. It is doubtful, however, that the vestibular portion of the nerve could not be completely destroyed without destruction of the cochlear portion.

The operation on the saccus endolymphaticus deserves mention, as suggested by Portmann.[8]

In cases where hearing should be preserved, dorsal sympathectomy[9] is to be considered and when done by the posterior approach[10] there is less likelihood of a postoperative intercostal neuritis.

Lempert[11] recommended a decompression operation for hydrops of the endolymphatic labyrinth. Rosen[12] suggested surgical division of the chorda tympani nerve, basing rationale on the notion that afferent nerves in the chorda tympani exercise some autonomic control over the vascular system in the inner ear.

Surgical treatment in Ménière's disease is indicated only in those cases which do not respond to medical treatment, such as nicotinic acid, Bellergal, thiamine chloride, small doses of potassium iodide, salt-free diet and a cessation of smoking, omission of alcohol and a normal routine of living without undue excitement, tension, or loss of sleep.

Patients who have had a fair trial on medical treatment, who have persistent attacks of severe dizziness with loss of useful hearing in the ear involved, with fair or good hearing in the opposite ear, justify the surgical approach for immediate and lasting relief from labyrinth dizziness arising in that particular ear.

It is interesting how simple the approach to the labyrinth can be made. In my first attempt[13] in 1939 I approached the labyrinth and ruptured the utricle and later reported four cases in the Laryngoscope in 1943, and in a series of 22 cases since that time I have attained sufficient confidence in the procedure used to present it here in detail as a direct and easy method to follow for the relief of Ménière's disease, where surgery is indicated.

I prefer and have found local anesthetic very satisfactory in all of my cases. Usually the patient is given 1½ grains of sodium

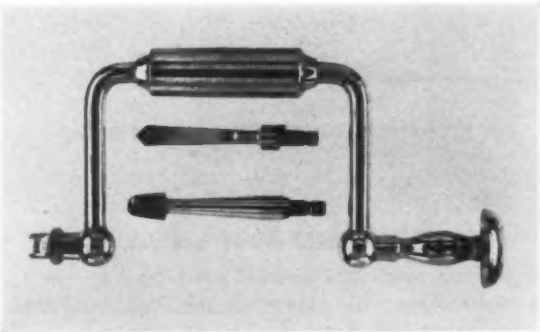

Fig. 1.—Hudson brace, perforator and Adson bur.

nembutal one hour before operation. An injection of 1/6 grain (10 mg) of morphine and 1/150 grain (0.4 mg) of Scopolomine® is given intramuscularly forty minutes before operation.

The usual surgical preparation is made to the skin and external auditory meatus followed by an injection of 1 per cent solution of novocaine, containing 10 drops of adrenalin (1:1000) per ounce. Care is taken to inject deep along the posterior wall of the canal. The postauricular incision is made 1 cm posterior to the mastoid auricular crease, carrying the primary incision through the periosteum, extending from a level of the superior attachment of the ear down to the tip of the mastoid bone but not beyond.

The skin and periosteum are elevated and pushed forward exposing the posterior and superior borders of the auditory canal.

The cortex is opened by means of a Hudson brace and bit, followed by an Adson bur (Fig. 1).

Here I wish to emphasize the importance of the Hudson brace and perforator which is routinely used as standard equipment by the neurosurgeons in doing brain surgery. Once this instrument is used and mastered it will be found that it is unsurpassed for opening the mastoid cavity and exposing the semicircular canals. It is un-

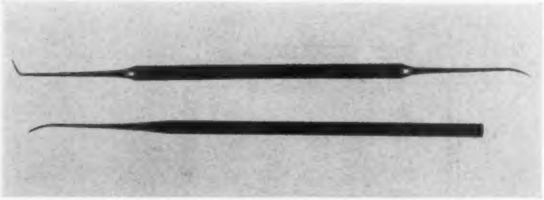

Fig. 2.—Dental explorer and pick.

surpassed in radical or modified radical mastoidectomies, whether done by the posterior or endaural approach. It is faster than the electric bur and gives a wide open clean cavity without alarming or unduly annoying the patient under local anesthesia. By means of this instrument, once the cortex is uncovered, the horizontal semicircular canal can be exposed in the matter of a few minutes.

The neurosurgeon is amazed that so few otologists are familiar with the use of this instrument which to them is paramount in surgery of the skull. After the mastoid bone is exposed the perforator is held firmly and turned several times back and forth through a quarter circle to start the perforation. This primary point is approximately 1 cm posterior to the posterior canal wall and approximately 1 cm below the level of a line extending posteriorly from the superior canal wall. Should the dura of the middle fossa or the lateral sinus be exposed, it will not be injured by the perforator or bur.

Upon the exposure of the horizontal canal, bone is removed forward by means of a Spratt curette, exposing the tip of the short process of the incus. Any bone chips are removed without irrigation. By means of a small sharp Spratt curette the anterior end of the horizontal canal is opened by stroking this area from before posteriorly until the canal is open, including the posterior portion of the ampulla. Through this opening is passed a small dental explorer or pick (Fig. 2) through the ampulla and into the vestibule. The pick is swept forward and then back toward the junction of the superior and lateral canals and withdrawn from the opening. The

periosteum and skin are closed by through and through silk. No attempt is made to irrigate the wound, nor is any medication or bone pressed into the canal.

The mastoid area is bandaged and the patient returned to bed where 50 mg of Dramamine® is given hypodermically three times a day.

The patient is given toilet privileges and the permission to get up as soon as he or she feels able. My last patient was up on the afternoon of operation and with Dramamine® hypodermically, continued to be up each day, leaving the hospital on the fifth day.

All of my patients have been able to leave the hospital by the fifth or sixth day and there have been no complications evident in any of these cases, even though no antibiotics or sulfa drugs have been used in this series of cases. Thus, it is evident that one can open the labyrinth without great danger of complications, if careful aseptic technique is followed, even without the use of antibiotics which may be used if desired.

I have noted that the opening in the canal fills with blood immediately and coagulation usually occurs within five to ten minutes, thus closing this opening. Schandler[14] says it is the hemorrhage into the perilymphatic space at the time of surgery which is followed by a sero-fibrinous labyrinthitis which destroys the inner ear.

So delicate is the vestibular membrane that no procedure other than the wide rupture of the membrane is necessary for its complete destruction.

The utricle is a very thin, frail, membranous sac which hangs in the posterior part of the vestibule. Just beneath the entrance of the double ampullae of the superior and lateral canals lies that portion of the utricle which bears its macula or "patch" of sensory epithelium. At operation the sweep of the explorer through the vestibule must destroy this membrane. However, any wide communication established between the endo- and perilymphatic spaces would undoubtedly destroy the functions of the endolymphatic membranes of both the utricle and saccule which are so delicately hung in the vestibule.

The horizontal canal is approximately 1 mm[15] in diameter and is completely walled off by blood and a fibrous clot within five to ten minutes after operation.

In my series of 22 cases there has been complete loss of hearing and vestibular function. There has been some disturbance of balance, however, for some months, especially when the patient suddenly looks upward.

SUMMARY

A brief survey of surgical methods used in the treatment of Ménière's disease is presented.

A neurosurgical approach to the labyrinth by the use of a Hudson brace, perforator and Adson bur is emphasized.

A simple method of destroying the endolymphatic membrane of the utricle and the establishment of a communication between the endolymph and perilymph is depicted.

The use of Dramamine® (50 mg) three times a day, hypodermically, following operation is recommended.

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XLI

TRACHEAL AND BROCHIAL PAPILLOMATOUS IMPLANT SHOWING MALIGNANT CHANGES

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CASE REPORT

G. F., a boy ten years of age, was first seen in the Department of Otolaryngology, Toronto General Hospital, April 1948, suffering with dyspnoea which required an immediate tracheotomy. The history revealed that he first became hoarse at the age of seven years, a diagnosis of multiple papillomata of the larynx was made and between the years 1945 and 1947 he had 9,000 r by teleradium to his larynx in another hospital, with little or no benefit.

Between April 1948 and September 1950, the patient was admitted to our department with recurrence of the papillomata which were removed on each occasion with biting forceps. In September 1950, he was admitted to hospital because of severe cough and dyspnoea. X-rays of the chest were negative. Laryngoscopic examination revealed multiple papillomata on the true and false cords with extension upwards on the epiglottis. Bronchoscopy was carried out through the tracheotomy opening, revealing small implants on the posterior tracheal wall, extending from the level of the tracheotomy opening to just above the level of the carina. Another implant was seen measuring about one-half cm in diameter on the medial wall of the left main bronchus just below the carina; this was removed with biting forceps. A course of aureomycin therapy was given and when discharged he showed some improvement. In January 1951, the patient was admitted because of severe dyspnoea. Bronchoscopy was essentially the same as on previous examination except an implant had developed on the medial wall of the right main bronchus just below the carina. An x-ray of the chest at this time showed evidence of early obstructive emphysema. In consultation with the medical department, a course of ATCH was given without effect. In April 1951, the patient was again admitted to hospital because of

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dyspnoea. Bronchoscopy revealed numerous implants in the areas before described; these were again removed with biting forceps.

In September 1951, the patient was admitted to hospital because of attacks of dyspnoea. Bronchoscopy revealed that there had been a recurrence of the implants but at this time the pathologist's report revealed that malignant changes had now taken place, characterized by invasion of the basement membrane, with down growths of tumor masses. The cells showed irregularity with pleomorphism and hyperchromaticism. Numerous admissions followed in 1952 and 1953 because of attacks of dyspnoea. Following the report that malignant changes had taken place in these implants, it was thought that diathermy applied to the base of these implants might be of value, this was carried out on several occasions without any beneficial results.

In January 1954, the patient, now sixteen years of age, was admitted to the hospital, almost exsanguinated following a severe pulmonary hemorrhage. An immediate transfusion of 1500 cc of whole blood was given. Fifteen hours following hospital admission, the patient had a massive pulmonary hemorrhage and died. Unfortunately, an autopsy could not be obtained.

SUMMARY

A case of multiple papillomata of the larynx is reported for which the patient received 9,000 r by teleradium without beneficial result. Five years later implants were found in the trachea and bronchi which showed malignant changes, the patient eventually dying from a massive pulmonary hemorrhage.

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(Scientific papers of the American Otological Society to be continued.)

The Scientific Papers of the American Broncho-Esophagological Association

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XLII

CARCINOMA OF THE BRONCHUS WITH NEGATIVE X-RAY FINDINGS

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and

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Despite the advances that have been made in techniques in thoracic surgery, the rate of cure of bronchogenic carcinoma still remains discouragingly low. This situation exists in spite of substantial increases in routine chest surveys that are being performed throughout the country and improvements in methods of diagnosis. Overholt and Schmidt[1] have stated that the rate of cure is 40 per cent if the lesion is discovered early and surgical resection can be performed while it is confined to the lung. Unfortunately, however, in a series of 721 patients observed by these authors, the disease was found localized in the lung in only 9 per cent. The rate of cure reported by most authors is 4 to 5 per cent of all cases of bronchogenic carcinoma. These figures practically parallel those of carcinoma of the stomach.

In view of the fact that the incidence of bronchogenic carcinoma seems to be increasing and that there is so much general interest in this disease at present, a reappraisal of the role of the bronchoscopist in this problem seems worthy of reconsideration. As is the rule in all neoplastic diseases, the principle problem in bronchogenic carcinoma is one of very early diagnosis, or to state it more correctly, the recognition of the early lesion. The method upon which most reliance generally is placed for the investigation of bronchogenic carcinoma is roentgenography of the chest. In view of the frequency with

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which x-ray examination is carried out in various broncho-pulmonary complaints, it would seem that this method of diagnosis in the already symptomatic patient is not the means whereby we can hope to reduce significantly the rate of cure of bronchogenic carcinoma. In recent years, we have been impressed by the fact that we have seen and heard of a significant number of advanced carcinomas of the bronchus in the presence of negative x-ray findings. This suggested to us that very early lesions of the large bronchi often may fail to produce significant roentgen changes. We, therefore, have undertaken to evaluate the relative merits of roentgen examination as compared to bronchoscopic investigation for the purpose of recognizing early cases of bronchogenic carcinoma.

As McCrae, Funk and Jackson[2] have stated, the early symptoms of bronchogenic carcinoma usually are those of bronchial irritation, while the early signs are those of bronchial obstruction. It is upon these two manifestations that the crux of the diagnosis of early lesions rests. The method of investigation which will reveal the presence of carcinoma when symptoms exist, in the absence of signs of obstruction, seems to offer more hope of improving the rate of cure of this disease. However, unfortunately, the diagnosis of bronchogenic carcinoma at present usually awaits the onset of signs of bronchial obstruction.

Graham,[3] Overholt and Schmidt[1] and Parker[4] emphasize the pitfalls in the investigation of the patient with bronchogenic carcinoma. The orthodox methods usually used to determine the cause of broncho-pulmonary symptoms are in order of their sequence: 1) history and physical examination, 2) roentgen examination and 3) bronchoscopic examination. The average patient waits three or more months after onset of symptoms before seeking the advice of his physician. After a course of medication fails to relieve symptoms, or immediately, the physician will request an anterior-posterior and sometimes also a lateral roentgenogram of the chest. It is at this time that the delay in establishing a definite diagnosis frequently begins. Graham and others have stated that there are no pathognomonic roentgen signs of bronchogenic carcinoma. Often the early diagnosis is suspected to be inflammatory disease and a course of antibiotic therapy is instituted. Jenkinson and Hunter[5] recognized the difficulty of establishing the early roentgen diagnosis of bronchogenic carcinoma. They demonstrated that one of the most common characteristic features of this disease is its tendency to simulate other conditions. Some time after x-ray films are made, the patient is likely to be referred for bronchoscopy. The average duration of time between the first visit of the patient to a general practitioner and the establishment of the diagnosis

of bronchogenic carcinoma is seven months. By then the cancer too often has become non-resectable.

ROENTGENOGRAPHY IN BRONCHOGENIC CARCINOMA

It is of interest that one finds in the literature different points of view concerning the role of roentgenography in the diagnosis of bronchogenic carcinoma.

Churchill[6] and Rigler[7] emphatically stated that it would be a rare occurrence to make a diagnosis of cancer of the lung in the absence of abnormalities discernible in the x-ray film. Rigler[8] claimed further that in most instances x-ray evidence of an abnormality would be present before the onset of respiratory symptoms in cases of bronchogenic carcinoma. He listed four roentgen abnormalities which are significant, but are frequently overlooked in lung cancer. They are: segmental or general pulmonary emphysema, minor differences in the size of the root shadow of the two lungs, linear areas of atelectasis, and a nodule in the periphery.

Allbritten and associates[9] presented the point of view that lung cancer would be missed only rarely if multiple roentgenograms were made. They stressed the value of inspiratory and expiratory positions and oblique views. In their series of 429 consecutive cases of cancer of the lung, using this technique, roentgen films were reported as normal in nine instances.

Carr and associates[10] in a thorough discussion of primary neoplasms of the lung also developed the thesis that evidence provided by thorough x-ray investigation may point to the existence of a neoplasm only indirectly, as for instance, by showing atalectasis, emphysema or pleural fluid. They were of the opinion that absence of a shadow was insufficient reason to rule out the existence of a lung tumor when suggestive symptoms were present.

Moersch[11] emphasized the value of x-ray examination in the study of patients exhibiting early signs of the disease, particularly hemoptysis. But he indicated that further investigation must be carried out when x-rays are uninformative. He also stressed the fact that a normal roentgenogram of the chest did not eliminate the possibility of the existence of a pathologic lesion.

Delarue[12] has stated, as have others, that unmistakable signs of bronchogenic carcinoma in the roentgenogram often do not appear when an early lesion is situated near the hilum. He pointed out that it is only after the malignant neoplasm has progressed in size sufficient to cause atalectasis, or has spread so as to produce glandular

enlargement, that incontrovertible x-ray signs appear. It was his opinion that one could not depend on routine chest films to detect early central lesions. The less frequent peripheral type of lesion, however, can be recognized in the roentgenogram at a relatively early stage because of its tendency to produce the so-called "coin shadow."

Overholt and Schmidt[1] reviewed the statistics of the results of many x-ray studies of the apparently well population. Approximately 10 in 100,000 cases will have shadows in the roentgenogram which will prove to be carcinoma. Blades[13] does not believe that such surveys always deal with patients who are asymptomatic. Careful questioning may reveal that a worrisome cough induced such patients to visit the survey unit. He deplored the factor of economy basic to these surveys, namely, miniature films and speed. Blades, however, did mention that 70 per cent of truly asymptomatic patients with positive x-rays who are explored promptly will have lesions with no lymphatic spread or metastases. On this fact is based the present belief that routine chest plates taken binannually will detect asymptomatic tumors.

BRONCHOSCOPY IN BRONCHOGENIC CARCINOMA

Bronchoscopic investigation provides the most certain method available, other than thoracotomy, for the diagnosis of bronchogenic carcinoma. The diagnosis can be established either by histopathological examination of biopsied tissue or by a study of bronchial secretion for exfoliated malignant cells according to the Papanicolou technique, as has been suggested by Herbut and Clerf.[14] This latter method has been a significantly important contribution which has improved both the opportunity and ability of the bronchoscopist to diagnose the early lesion.

The value of direct inspection of bronchial carcinoma was emphasized by McCrae, Funk and Jackson.[2] They stressed the importance of a thorough knowledge of the normal appearance of the tracheobronchial tree in order to recognize the minor alterations suggestive of the early neoplastic lesion. Color, form and fixity were mentioned as the three criteria that must be entirely familiar to the endoscopist.

Overholt and Rumel[15] have listed bronchoscopy as the most valuable single diagnostic procedure in the study of patients suspected of having primary carcinoma of the lung. They demonstrated that bronchoscopy will prove effectual for the diagnosis of early lesions in the stage of irritation manifested by cough and increased secretion; in other words, in the stage before bronchial occlusion.

Wierman, McDonald and Clagget[16] in a recent provocative contribution described five cases of squamous cell carcinoma of the major bronchi that were resected in which there was no apparent gross tumor formation. X-ray examination was negative in two of these cases. One of the lesions was a carcinoma in situ and the others were small superficially invasive growths with surrounding areas of in situ carcinoma. The authors expressed the belief that all cases of bronchogenic carcinoma probably originate as in situ lesions. They were able to indicate in these cases an alteration of the normal mucosal pattern that appeared as a series of longitudinal furrows or grooves in the mucosa of the main, secondary and, partially, tertiary bronchi. These normal ridges are formed by irregularly placed submucosal smooth-muscle bundles. The mucosal changes in the cases described were due to the tendency of the carcinoma in situ to proliferate centrifugally, extending into the longitudinal grooves and obliterating them. This obliterative process may be associated with a wrinkling, granular or nodular appearance of the mucosa. These authors stated that an appreciation of this altered mucosal pattern can aid significantly in the endoscopic detection of bronchogenic carcinoma even though the tumor may not be seen.

Kramer and Som[17] analyzed the bronchoscopic aspects of 300 cases of carcinoma of the lung. In their series, 74 per cent of the cases yielded positive biopsy findings. Also, 62 per cent of the cases arose from a bronchus of the first, second or third order, 18 per cent from small branch bronchi and 20 per cent from terminal branchioles or parenchyma. According to these authors, lesions originating in the mucosa grow by direct extension and through the lymphatic system producing either local intrusion into the bronchial lumen or ulceration of the mucosa. Early lesions were suspected by thickened spurs, nodular mucosa, flat elevations and evidence of infiltration.

Rabin, Selikoff and Kramer[18] have stressed the importance of paracarinal biopsy in evaluating operability of cases of bronchogenic carcinoma. In their series of 154 cases, the paracarinal mucosa appeared normal endoscopically but demonstrated evidence of submucosal carcinomatous extension on biopsy in 16 instances.

The following brief case presentations are illustrative of advanced bronchial carcinomas in the presence of negative conventional x-rays. These patients were bronchoscoped by one of us (J. L. G.) during the past four years.

REPORT OF CASES

CASE 1.—T. H., a 70 year old white male was admitted to the Medical Service of The Mount Sinai Hospital because of hemoptysis

of three days' duration. Seven and one-half months prior to admission, the patient suffered an episode of hemoptysis which persisted for several weeks.

X-ray examination revealed evidences of an old tuberculous lesion in the upper portion of the right lung. The original films revealed no evidence of disease of the left lung. Questionable atalectatic areas, which developed while the patient was in the hospital, were attributed to the bronchial bleeding.

On bronchoscopy a considerable amount of blood was seen issuing from the left lower lobe bronchus. After the bleeding had been controlled, an irregular, reddish mass was seen arising from the wall of the bronchus. Histopathological examination of the tissue that had been removed revealed this to be a squamous cell carcinoma.

An emergency left pneumonectomy was performed because of continued severe bleeding. Pathological examination of the resected lung revealed the presence of a polypoid squamous cell carcinoma of the left bronchus with extension through the bronchial wall at the hilum. No metastatic lymph nodes were found.

The patient lived for 18 months.

Case 2.—C. R., a 68 year old white male, was admitted to the Private Service of Dr. David Beck at The Mount Sinai Hospital because of cough and hemoptysis of eight months' duration. Repeated roentgenograms of the chest had been reported as negative.

Bronchoscopy revealed large amounts of blood arising from the left lower lobe bronchus. The mucosa of this bronchus in the region of the anterior-basal branch was granular and irregular. Biopsy taken from this site was reported as squamous cell carcinoma. Paracarinal biopsy was negative.

Pathological examination of the excised lung revealed a squamous cell carcinoma of the left lower lobe bronchus with infiltration of the bronchial wall and direct invasion of the lymph nodes.

This patient died six weeks after operation as a result of acute pericarditis.

Case 3.—B. M. B., a 72 year old white male was admitted to the Private Service of Dr. Herman Hennell at The Mount Sinai Hospital because of daily small hemoptyses of three weeks duration. A roentgenogram revealed no abnormality; fluoroscopy disclosed slight displacement of the mediastinum toward the left side on inspiration, suggestive of partial bronchial obstruction.

Bronchoscopy revealed an irregular, reddish mass involving the walls of the left lower lobe bronchus. This proved to be a squamous cell carcinoma on histopathological examination. Paracarinal biopsy was negative.

Examination of the resected lung revealed an infiltrating and obstructing carcinoma of the left lower lobe bronchus. One of the removed mediastinal nodes contained carcinoma cells.

This patient lived for 15 months.

DISCUSSION AND SUMMARY

The chief reason for the low rate of cure of cases of bronchogenic carcinoma is usually that the lesion already has extended beyond the confines of the lung by the time surgical intervention is undertaken. Conversely, a higher rate of cure results when the carcinoma is limited to the lung alone. However, it is our impression that the optimism which now exists on the part of some concerning the chances of cure because of current methods of diagnosis and treatment will not be realized if there continues to be so much reliance placed upon roentgen diagnosis, particularly if conventional positions are employed for the recognition of early lesions. Although the incidence of carcinoma of the bronchus in the presence of negative x-rays as demonstrated by our present diagnostic methods is small, we nevertheless have been impressed not only by the fact that such lesions do exist, but that they are not infrequently already quite advanced. We believe that the incidence of negative x-rays would be much higher if early lesions in the symptomatic patient could be detected in the initial stages of the disease.

In spite of this point of view, we feel that complete roentgen study is indicated in every case in which symptoms of bronchial irritation are present even for a few weeks. To obtain as much diagnostic information as roentgenography can offer, however, such study always should include the taking of lateral, oblique, and inspiratory and expiratory films. In this manner, indirect information which will lead to the suspicion of the presence of a bronchogenic carcinoma probably will be revealed much more frequently than at present.

The basic fact involved in a discussion of the relative merits of roentgenograph and endoscopy in the diagnosis of carcinomas involving the larger bronchi is that direct endoscopic observation offers greater possibilities of detecting the early lesion than even the most careful x-ray studies. Bronchoscopy offers the opportunity of de-

tecting early lesions by securing adequate biopsies and secretion for cytologic examination. This opportunity is enhanced by the fact that the majority of bronchial carcinomas usually are located in the bronchi of the first three orders. Short of thoracotomy, this is the only definitive method of establishing the existence of a lesion at an early stage of the disease. Although this knowledge is not new, the present low rate of cure of bronchogenic carcinoma clearly indicates that endoscopic diagnostic procedures perhaps are not performed sufficiently soon in symptomatic patients with evidences of bronchial irritation.

The bronchoscopist has a personal responsibility in this problem. He must be familiar with the early alterations in normal bronchial mucosa and bronchial architecture so that the correct site of biopsy of the early lesion is chosen. He must also be trained to detect the precise source of bronchorrhea so that the correct sample of secretion for cytological study is obtained. It is evident that the well-trained bronchoscopist through his specialized knowledge is prepared to make his contribution to the diagnosis of bronchogenic carcinoma at an early stage of the disease. He, therefore, is an important member of the team of physicians who can attempt to improve the rate of cure of cases of bronchogenic carcinoma.

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XLIII

A THIRTY-ONE YEAR HOSPITAL EXPERIENCE WITH THE BRONCHOSCOPIC APPROACH TO BRONCHIAL ADENOMA

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Since 1923, 53 patients with carcinoid adenomas and three with cylindromas have been diagnosed or treated by bronchoscopic means at the Massachusetts General Hospital. Three patients with carcinoid adenomas and one with a tracheal cylindroma included in a previous study have been excluded from this paper because they were never treated by bronchoscopy.[1] The pathology has been carefully reviewed. Only those growths which were completely identifiable histologically as falling into these two groups have been included. Several which were originally called carcinomas were found to be carcinoid adenomas as a result of this study.

Evidences of malignancy were hard to find among the carcinoid adenomas. All were grossly circumscribed. No blood vessels were invaded by tumor and there were no distant metastases. Occasional mitotic figures were found, some tumors showed evidence of microscopic invasion of the tumor capsule; two had metastasized to single adjacent lymph nodes and, in one of these tumor was found in a lymphatic channel.

The cylindromas were quite different pathologically. All were invasive and formed no capsule. Mitotic figures were more frequent. Extensive lymph node metastases were found at autopsy in one patient in this group whose tumor had recurred 13 years after pneumonectomy. It had caused his death by widespread invasion of mediastinal structures. No distant metastases and no blood vessel invasion were found in these patients, but there was ample evidence of lymphatic invasion.

The follow-up in all cases has been complete. Thirteen of the patients with carcinoid adenomas have died. Although only eight were examined by autopsy the causes of death for the remaining five are known and apparently none died of his disease. Two of the patients with cylindromas have died, both were examined at autopsy,

both died of their disease. Forty-one patients are living. Three still retain their carcinoid adenomas because their general physical condition renders them poor operative risks for thoracic surgery. There is no evidence as yet of local or distant metastases among the living patients. Only the three whose tumors are still present have symptoms.

In general, bronchoscopic observation and biopsy were invaluable in establishing the diagnosis of adenoma. Because most of these tumors arise in major airways they are usually readily accessible to the endoscopist. Actually, however, because many of the carcinoid adenomas were first seen on an average of four years after the onset of symptoms, the readiness with which they were observed depended to some extent upon the fact that they were probably much larger than they had been when symptoms began.

As a result of careful dissection of lung tissue removed surgically or at autopsy, 11 our of the 53 carcinoid adenomas in this series were found to have their site of origin in the secondary division of a lobar bronchus. Had the patients been studied by bronchoscopy earlier in the course of their disease many of their tumors might not have been seen. Only as some of these grew and protruded into lobar bronchi did they become available for bronchoscopic observation. Seven were diagnosed by bronchoscopic means, four others were too peripheral to be seen. Two of this later group, in addition, lay completely outside of the bronchial wall from which they had arisen. Four more tumors (arising in major bronchi) were missed initially at bronchoscopy. Three, however, were identified subsequently by this means. The patient with the fourth tumor was not studied by bronchoscopy again. The blood and secretions which obscured her adenoma issued from a lung abscess which was treated by pneumonectomy. Five other carcinoid adenomas were seen through the bronchoscope but biopsies were not performed. Four were called adenomas. The fifth, which lay in the right upper lobe bronchus was called a carcinoma. This error of observation and failure to obtain a biopsy had no unfortunate sequelae because the patient was too old (76) to undergo any resection more extensive than a lobectomy. Forty-three carcinoid adenomas and all three cylindromas were correctly diagnosed by biopsy on initial bronchoscopy. In Fig. 1 the position of these tumors in the bronchial tree is shown schematically. The effectiveness of the bronchoscope as a diagnostic tool is portrayed in Table 1. In an era when many so-called "coin lesions" and other roentgenographic shadows can only be diagnosed by transthoracic exploration, the adenoma stands out as an example of a tumor which can usually be easily and accurately diagnosed bronchoscopically with little risk or suffering on the part of the patient.

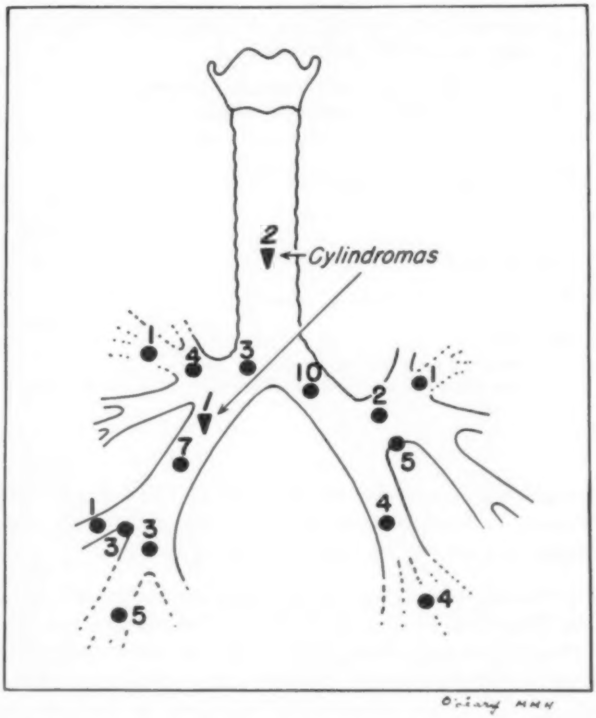

Fig. 1.—Schematic presentation of the location of 53 carcinoid and three cylindroid adenomas in the tracheo bronchial tree.

EVALUATION OF TRANS-BRONCHOSCOPIC RESECTIONS

1. *As a Means of Achieving Complete Cure.* Even before Kramer identified the adenoma as a pathologic entity in 1930, endoscopists were attempting to resect it and other tumors through the bronchoscope.[2] This form of therapy continued to be popular during the period when the adenomas were considered to be endobronchial lesions of a non-maligant nature. The hazards of thoracic surgery, furthermore, were sufficiently great during the 1930's that surgeons hesitated to perform pulmonary resections except for severe hemorrhage or uncontrollable infection. By 1945, however, both the technical difficulties involved in effecting complete bronchoscopic extirpation of the carcinoid adenoma and its malignant potential were

TABLE 1.—EFFECTIVENESS OF BRONCHOSCOPIC OBSERVATION AND BIOPSY IN DIAGNOSING BRONCHO-TRACHEAL ADENOMAS.

53 Patients with Carcinoid Adenomas
3 Patients with Cylindromas

Diagnosed by trans-bronchoscopic biopsy	46 (3 were cylindromas)
Presumed to be adenoma on observation	4
Presumed to be carcinoma on observation	1
Not seen (4 were too peripheral to be seen, 1 was small and obscured by bleeding.)	5

well enough understood that in our hospital this form of treatment was relegated to the palliation of symptoms in patients who could not be expected to survive transthoracic resections.

In reviewing the tumors encountered in this series it is interesting to see what was possible in the way of endoscopic cure from the technical and pathologic viewpoints. None of the cylindromas could have been entirely removed endoscopically. All three had grown through the wall of the airway. In addition, one had extended the full length of the trachea and one had metastasized to the regional lymph nodes. The third, which occupied only a small area of the the trachea, was excised through the bronchoscope, but because of recurrence a partial tracheal resection was necessary two years later.

Conditions were only slightly more favorable for the removal of the 53 carcinoid adenomas. From the technical viewpoint complete endoscopic excision was impossible for 45 of these. Forty were largely extrabronchial. Four others were too peripheral to be seen. One more of those which could be seen was attached at a point so far within the superior segmental bronchus of a lower lobe that it could not be entirely resected. Penetration of the tumor into or through the bronchial wall was found microscopically in five polypoid adenomas. Cauterization or electrocoagulation might, of course, have destroyed such limited extensions of tumor. Single lymph node metastases were found in two cases. In one it was associated with an intraluminal adenoma.

TABLE 2.—POSITION OF CARCINOID ADENOMAS IN RELATION TO THE BRONCHIAL WALL, OCCURENCE OF PATHOLOGIC CHANGES IN LUNG TISSUE DISTAL TO THEM AND OF METASTASES WHICH PREVENTED COMPLETE CURE OF 53 CARCINOID ADENOMAS BY ENDOSCOPIC RESECTION OF THE TUMORS ALONE.

FACTORS	NO. CASES
Tumors inaccessible or extending extramurally	48 (3 were cylindromas)
Lymph node metastases	3 (1 was a cylindroma)
Uncontrollable pulmonary infection	47 (1 was a cylindroma)
Completely intraluminal and without distal pathologic changes	1

Among the five intraluminal lesions which were technically available for bronchoscopic resection, irreversible pulmonary infection in the lung tissue distal to the tumors was observable in four. Although chronic infection in the lung tissue beyond a tumor may not be a contra-indication to local removal, the chances of complete symptomatic relief by such a procedure are slight. Out of the 53 patients with carcinoid adenomas only six had no demonstrable evidence of permanent pathologic changes in the pulmonary tissue distal to the tumor. Among the remaining 47, 32 had bronchiectasis, 19 had chronic pneumonitis, 9 had empyema and 4 had lung abscesses. These occurred separately or in combination. Because most of these patients had had symptoms for a number of years prior to their initial bronchoscopies (four years on an average) it is probable that even when they were first seen their infectious processes were not reversible. These findings have been summarized in Table 2. In only one patient out of 53 was a complete cure possible by endoscopic resection.

Actually, since the first patient entered the Eye and Ear Infirmary in 1923 for bronchoscopic excision of her carcinoid adenoma, a total of 20 have received such treatment. Eleven were treated in whole or in part at other hospitals, a fact of some importance because they were referred usually for transthoracic resections after

TABLE 3.—20 PATIENTS WITH CARCINOID ADENOMAS TREATED BY ATTEMPTED TRANSBRONCHOSCOPIC RESECTION.

Total number of bronchoscopies (approx.)	305
Least per patient	2
Most per patient	75
Average per patient	15.2
Years of Therapy per Patient:	
Least	0.2
Most	14
Average	3.5

hope of endoscopic cure had been abandoned. These 20 patients have been studied according to how much their illnesses were prolonged and complicated by the postponement of definitive surgery, the mortality of therapeutic bronchoscopy, the results in terms of actual tumor removal and finally the over-all survival from the time of diagnosis.

Although for a few of these patients the course of treatment was brief, for most it went on for years. Repeated bouts of infection and hemorrhage and multipe hospital entries for bronchoscopy were involved. In brief a total of approximately 305 endoscopic procedures including resection, cauterization, coagulation, implantation of radon seeds and simple observation were performed upon these 20 patients. The least per patient was two, the most 75. The shortest course of therapy was just under two months, the longest over 14 years. The average number of procedures was 15 per patient over a 3½ year period (See Table 3).

Nor were the procedures entirely harmless. One patient died from hemorrhage on the operating table during her 14th bronchoscopy. One died of bleeding at home five days after her 13th bronchoscopy. Both of these deaths were probably avoidable. In each case the tumor completely occluded the opening of a main bronchus and had caused total collapse and bronchiectasis throughout the lung beyond, rendering it useless. Both patients, therefore, had limited pumonary reserves and could not be expected to tolerate much aspiration of blood into their normal lungs. The following measures might avoid fatalities under similar conditions: First, avoidance of

TABLE 4.—RESULTS OF ATTEMPTED TRANSBRONCHOSCOPIC RESECTION OF 20 CARCINOID ADENOMAS.

	RESIDUAL PULMONARY INFECTION	DIED	SUBSEQUENT TRANSTHORACIC RESECTION
Cured (1)	0	0	0
Complete local removal (4)*	4	1	3
Incomplete removal (15)	14	3	12
Total (20)	18	4	15

*In 1 patient a single lymph node metastasis was found at autopsy.

the use of cough-repressing narcotics in the preoperative preparation of the patient; second, laying the patient on the side of the collapsed lung during the operative procedure; third, tipping the operating table into a marked head down position after insertion of the bronchoscope; fourth, avoiding the use of biopsy unless absolutely necessary. Additional safeguards would include typing and cross-catching the patient preoperatively, and having oxygen and cautery readily available. The first patient was autopsied and her death was found to have resulted from the aspiration of blood. Whether the other patient died of a similar cause is subject to conjective, as no autopsy was performed. The fatality in her case might been avoided, however, had she been kept in the hospital long enough to be certain that complete hemostasis had been achieved. Hemorrhage postoperatively has caused a fatality, however, despite observations on a hospital ward.[3]

In addition to the two operative deaths, two more patients died of pulmonary infection unrelieved by the attempted resections of their tumors. The first was a 21 year old girl who died of lung gangrene, pneumonia and empyema secondary to an adenoma of the left main bronchus which had been incompletely removed despite multiple bronchoscopic resections over a four year period. The second was a young man who underwent 28 bronchoscopic treatments and a short course of roentgen therapy over a four year period for an adenoma of the left main bronchus. Two years later he died of pneumonia. At autopsy no residual tumor was found in the bronchus but chronic pneumonitis, bronchiectasis, amyloidosis and a metas-

TABLE 5.—CARCINOID ADENOMAS. SURVIVAL FROM TIME OF INITIAL BIOPSY FOR 20 PATIENTS TREATED BY ATTEMPTED TRANSBRONCHOSCOPIC RESECTION.

Alive and well	12	
Dead	8	
Died of their disease	0	
Metastases	1	
Longest survival	27	years
Shortest survival	0.3	"
Average survival	9.8	"

tasis to a regional lymph node were encountered. This case has been previously reported by Holley.[4] All four deaths occurred in patients with tumors arising in a main bronchus, three on the left and one on the right.

Complete local removal of the tumor was effected in four other patients besides the one just referred to. In one a complete cure was achieved by three bronchoscopic resections and the insertion of radon seeds into the base of the tumor. There were no apparent pathologic changes in the distal lung tissue and the patient is alive and well 21 years later. The other three continued to suffer from severe infection and bleeding which came from bronchiectasis and pneumonitis in the lung tissue beyond their tumors. Pulmonary resections were necessary to relieve their symptoms. In none of the resected specimens was there any stenosis of the bronchus at the previous site of the tumor. The remaining 12 patients were subsequently treated by transthoracic resections after multiple bronchoscopies had failed to cure them of either their adenomas or their symptoms. These results are shown in Table 4.

The carcinoid adenoma as compared with bronchogenic carcinoma is slow to grow, slow to metastasize and in general well tolerated by the human body. The followup of the 20 patients treated bronchoscopically provides ample evidence of this. The shortest period of survival after diagnosis was four months for one of the patients who died of bleeding. The longest is 27 years for a patient who underwent 14 years of endoscopic procedures prior to a pneumonectomy. He is alive and well at the moment. The average period of survival has been over nine years. Twelve patients are still alive

TABLE 6.—SYMPTOMATIC RELIEF FOLLOWING PARTIAL OR COMPLETE TRANSBRONCHOSCOPIC RESECTION IN 22 PATIENTS WITH CARCINOID ADENOMA.

CHIEF COMPLAINT	NO. OF PATIENTS	AVERAGE DURATION OF RELIEF
Pulmonary infection	12	5 mos. to 6 yrs.
Hemoptysis	5	1 mo. to 5 yrs.
Cough	5	0 mos. to 22 yrs.

and well. Two died after pulmonary resections, both from infection, both before 1937. Two died less than three years after lobectomies, one from an adrenal carcinoma and one from a gastric carcinoma. All four were examined at autopsy. No residual adenoma nor metastases were encountered. In Table 5 the survival rates are shown.

2. *Brochoscopic Measures for Palliation of Symptoms.* Cylindromas are, as a rule, extensive infiltrating tumors which encircle the trachea or a major bronchus. Only one in this series presented itself as an intratracheal pedunculated mass which partially occluded the airway. Good relief of cough and inspiratory dyspnoea were obtained for over a year by resection of the projecting tumor.

The carcinoid adenoma is more apt to occlude bronchial passageways because a whole or a part of its bulk projects into the lumen. Cough, hemoptysis and symptoms secondary to bronchial obstruction are commonly encountered. Aspiration of secretions and reestablishment of the airway to the atelectatic lung beyond the tumor will often bring about immediate and dramatic relief. In addition to the 20 patients in whom complete resection of their adenomas was attempted bronchoscopically, two more patients were bronchoscoped a few times each in an attempt to give some symptomatic relief. Neither were considered to be adequate surgical risks for thoracotomy. In general, among this total of 22 patients, the improvement after most of the bronchoscopic procedures was encouraging. Prolonged relief, as a rule, depended on complete removal of the endobronchial portion of the tumor by repeated resections. This was even true for a few patients whose chief complaint was bleeding. Productive cough was more apt to diminish than to disappear after endoscopic resection. Symptoms of infection were subject to episodic recurrence if there was much bronchiectasis or pneumonitis present, but did not become persistent or severe until the adenoma grew back once more. Effective

symptomatic relief was achieved for one patient for six years, for another for four and several others had little complaint for a year or more. By and large the relief was transitory and had no direct relationship to the progression of the tumor. The palliative effects of bronchoscopic resection and aspiration have been outlined in Table 6.

CONCLUSIONS

A study of the use of the bronchoscope as a diagnostic and therapeutic instrument among 53 patients with carcinoid adenomas and three with cylindromas over a 31 year period has been presented. Although the cylindromas are nearly always observable on bronchoscopy, the carcinoid tumors are occasionally too peripheral or not sufficiently intraluminal to be seen. As a rule bronchoscopic biopsy is an invaluable diagnostic measure. A pathologic diagnosis in carcinoid adenoma is helpful when plans for the appropriate surgical resection are being made because these are tumors which can be cured by more conservative operations than would be effective in bronchogenic carcinoma. Despite the fact that favorable results have been reported by others in the treatment of the carcinoid adnoma by transbronchoscopic resection, the results of such treatment in 20 cases so treated in this series point to the opposite conclusion.[5] Among patients who are good surgical risks for transthoracic resections, endoscopic removal should not be attempted for the following reasons: First, the pulmonary infection beyond these tumors is usually a result of permanent pathologic changes which can only be cured by excision. Second, most of the adenomas are technically inaccessible for complete endoscopic removal . Third, no malignant tumor, even of low-grade malignancy should be subjected to any surgical procedure less than total excision under direct vision. For the cylindroma which is usually invasive, extensive and prone to metastasize, this is obvious. It is less so for the carcinoid adenoma. Although only two of these growths in this series had metastasized, ample evidence of lymphatic and blood vessel invasion as well as of distant metastases exist.[6, 7, 8] Fourth, the operative mortality of bronchoscopic resection and that from infection in lung tissue beyond the adenoma are by no means negligible. Four deaths from these causes occurred among the 20 patients in this series treated endoscopically, whereas there were only two postoperative deaths following 47 transthoracic and tracheal resections in the same hospital in the same period of time.[1] Fifth, the number of bronchoscopies and the number of years spent in treating patients by this means (an average of 15 procedures over 3½ years time for the 20 patients so treated) is unwarranted on the basis of prolonging suffering, cost and the danger of metastases.

The use of bronchoscopic aspiration and resection for relieving the symptoms of patients who cannot be expected to survive transthoracic resection or to relieve symptoms prior to thoracotomy is justified, effective and often compatible with prolonged survival.

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XLIV

BRONCHOGRAPHY WITH DIONOSIL

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and

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Three years go, in a paper before this Association,[1] the authors described their experiences with two relatively new aqueous contrast media. These preparations, Umbradil Viscous B and Ioduron B, had been introduced chiefly with the intent of avoiding the prolonged alveolar retention usually seen after instillation of iodized oil. In their essential constituents, the two products are identical, consisting of a 50 per cent solution of iodopyracet to which is added sodium carboxymethylcellulose sufficient to provide the desired viscosity. Among the advantages offered by these preparations, in comparison with the iodized oils, were listed their rapid elimination (usually in less than four hours), their stability, a viscosity which may be altered, and freedom from systemic toxic effect.

The use of these media, however, was found to entail certain difficulties, relating chiefly to the irritating quality of the solutions, a result of their marked hypertonicity. An elaborate technique of anesthesia was required, and even with this, coughing sufficient to interfere with completion of the examination occurs with some frequency. Bronchograms made with these preparations have in general been no more informative than those obtained with iodized oil, and in many instances have seemed less so, usually because of lack of uniform filling, inadequate filling of peripheral branches or rapid dispersion.

Accordingly, the use of aqueous solutions of iodopyracet was reserved chiefly for such indications as the study of obscure pulmonary disease or segmental localization of foreign bodies, in which rapid disappearance of the contrast substance is an advantage, and for the occasional cases of known sensitivity to iodine or inorganic iodides.

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With a view to finding a contrast substance which might be less irritating, yet still allow rapid elimination, Tomich, Basil and Davis[2] investigated the properties of the n-propyl ester of 3:5 di-iodo-pyridone acetic acid, whose diethanolamine salt is known in the United States as iodopyracet (Diodrast®), and in England as diodone. The propyl ester, known as propyliodone, because of its low solubility in water, allows the preparation of a 50 per cent aqueous suspension which is isotonic and therefore quite free of irritation when instilled into the bronchial tree. Thus has been eliminated the most objectionable feature of the aqueous media previously employed.

In the preparation known as Dionosil Aqueous, the 50 per cent suspension of propyliodone is combined with sodium carboxymethyl cellulose as a viscosifying agent, sodium citrate as a buffer, sodium chloride to render the suspension isotonic and a small amount of benzyl alcohol as a bacteriostatic. An oily suspension of the same substance, Dionosil Oily, is available in 60 per cent concentration with arachis oil as the vehicle. The size of the suspended particles is said to be in the range of 5 to 15 micra. Propyliodone may be sterilized by dry heat up to 150° C. for as long as two hours without decomposition. Since the iodine content of propyliodone is 58.6 per cent the net iodine contents of the aqueous and the oily preparations are about 30 per cent and 34 per cent respectively, i.e. somewhat less than that of the iodized oils, but greater than that of such aqueous solutions of iodopyracet as Umbradil and Ioduron.

Elimination of that portion of the contrast substance which is not expectorated occurs by hydrolysis, presumably enzymatic. The product of hydrolysis, a sodium salt of 3:5 di-iodo-pyridone acetic acid, is excreted by the kidney without further decomposition, so that iodism due to liberation of free iodine or inorganic iodides does not occur, and unfavorable effects due to iodine or iodide absorption in active tuberculosis need not be anticipated. The interval required for complete elimination of the contrast substance is short enough to meet practical requirements, usually not exceeding three days, but may be a little longer following instillation of the oily preparation.

Dionosil may be instilled by any of the conventional methods for bronchography, but to us the catheter method of intrabronchial instillation has seemed preferable, because it allows better control of the filling of successive portions of the bronchial tree, particularly when the procedure is performed under fluoroscopic observation.

The technique is essentially that described by Jackson and Bonnier,[3] with minor modifications. As pre-medication, the average patient is given codeine sulfate, 30 mgms, and atropine sulfate, 0.4

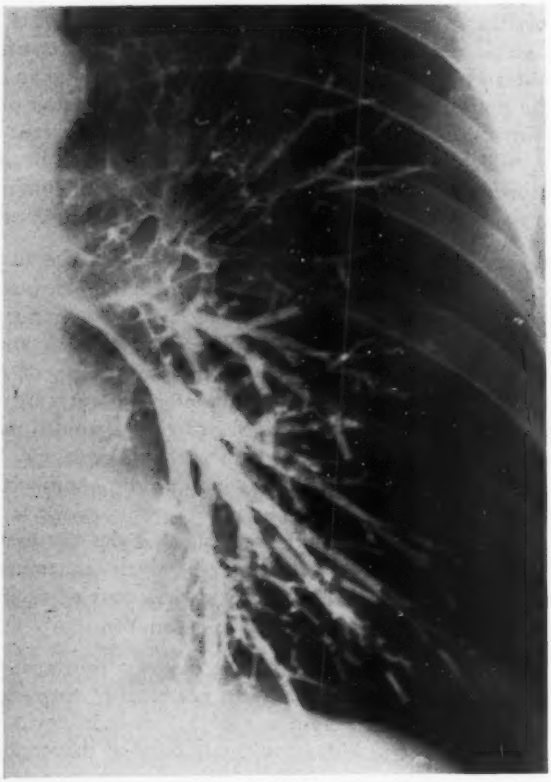

Fig. 1.—Bronchography with Dionosil Aqueous. Initial stage of filling in film made six minutes after beginning of instillation.

mgm, both hypodermically, and sodium pentobarbital 100 mgms by mouth, about 45 minutes before the procedure. Anesthesia is given with the patient sitting on the edge of the fluoroscopic table. The pharynx is sprayed lightly with 2 per cent pontocaine hydrochloride or 4 per cent cocaine hydrochloride, following which 1 ml. of 10 per cent cocaine is instilled, a few drops at a time, with a laryngeal syringe under mirror guidance. Then, favoring gravitation into the bronchial tree of the side to be mapped by having the patient incline his body after each instillation, 6 ml of xylocaine 2 per cent is instilled, 2 ml at a time.

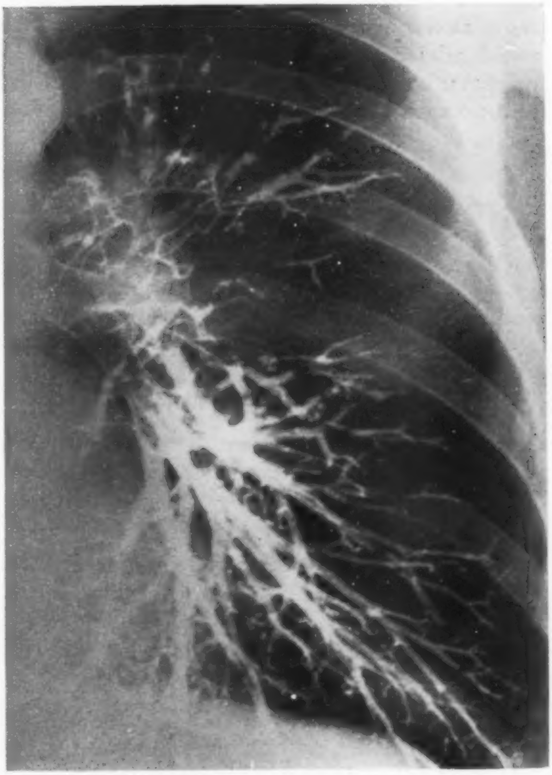

Fig. 2.—Later stage of filling (same case). Film made sixteen minutes after beginning of instillation. Note progression of filling to smaller peripheral bronchi, but absence of alveolar filling.

A Stitt catheter, No. 16 F., is then introduced through the larynx on a stilette under mirror guidance, and with the patient lying on the fluoroscopic table in the supine position, the catheter is positioned a short distance below the carina on the side to be filled. Next, with the patient lying on this same side, an additional quantity of 2 per cent xylocaine is instilled for effect in the upper lobe. Then, after an interval of three or four minutes, the instillation is begun under fluoroscopic guidance with the head of the table slightly lowered, so that the upper lobe is filled first. The table is then slowly raised, as the patient rolls forward and backward to fill all segments, the basal

segments usually being filled by the time the table has reached a vertical position. Finally, just before the films are exposed, the patient is seated on a stool and the head and shoulders lowered toward the floor as a small additional amount of suspension is injected to be sure that filling of the apical portion of the upper lobe will be complete. Films are then exposed in the ventral and oblique positions (stereoscopic) and in the lateral projection.

Several details in the technique concern particularly the use of Dionosil. Since the preparations are suspensions rather than solutions they should be well shaken just prior to the beginning of the instillation. The syringe is then filled by pouring the suspension into the open end of the barrel, and the plunger may be lightly lubricated to allow smooth action. The material should be instilled slowly, allowing about twice as long as in the case of iodized oil; the entire instillation usually requires 5 to 6 minutes. The volume of suspension used will avergae 15 ml for an entire lung.

If Dionosil Oily is to be used, smaller amounts of anesthesia solution are required. After all films are exposed, the patient is encouraged to cough and expectorate as much of the suspension as possible.

It has been gratifying to observe that although Dionosil Aqueous penetrates well to the small peripheral bronchi there is little tendency for alveolar filling, so that as much as twenty minutes may be allowed for the instillation and incident fluoroscopic observation if desired. It is not necessary to complete the instillation and expose the films with the rapidity essential in the case of the iodized oils.

Here is encountered a seeming paradox; since the viscosity of Dionosil Aqueous is considerably less than that of iodized oil, one would expect alveolar filling with greater rapidity and of greater degree. The explanation as to why this does not occur is lacking, although it has been speculated that precipitation of the suspended particles on the mucosal surface occurs with decreasing rate of flow near the periphery and with diminished thickness of the fluid layer coating the mucosa. Though rarely seen in bronchograms made with the aqueous preparation, alveolar filling may occur when Dionosil Oily is used, particularly if the rate of instillation and the amount used are excessive.

The bronchographic characteristics of Dionosil are indicated by the illustrative bronchograms. In Figure 1 and 2 are shown two stages in the filling of a relatively normal left bronchial tree with Dionosil Aqueous. The first film, exposed about six minutes after the beginning of the instillation, shows adequate peripheral filling of the upper

Fig. 3.—Bronchography with Dionosil Aqueous. Compression of right middle lobe bronchus with evidence of retained secretions ("middle lobe syndrome").

lobe bronchi, but a lack of peripheral filling in the subsequently filled lower lobe bronchial tree. In the film made 10 minutes later (16 minutes after the beginning of the instillation) there is still good definition of the smaller bronchi in the upper lobe, and the lower lobe now shows adequate peripheral filling, although there is no appreciable alveolar filling in either lobe.

There may be some tendency on the part of those accustomed to bronchography with iodized oil to complete the instillation and expose the films too rapidly. This will result in a bronchogram without adequate peripheral filling; such an error may be avoided by fluoroscopic observation until the smaller bronchi are seen to be well demonstrated, or by exposing a second set of films after an interval of about ten minutes. If flow toward the periphery seems too slow, deep breathing, as suggested by Don,[4] may be helpful.

In Figure 3 is shown the bronchogram with Dionosil Aqueous of a male of 37 years with chronic cough and expectoration. The initial roentgen examination had been negative, and the bronchoscopic findings essentially so. The bronchogram with Dionosil Aqueous likewise showed nothing striking in the postero-anterior projection, but the lateral view shows beginning compression of the proximal portion of the right middle lobe bronchus, presumably due to enlarged lymph nodes. Although there is no atelectasis, the lack of normal peripheral filling seen in other parts of the bronchial tree indicated the presence of retained secretions. This was classified as a case of middle lobe syndrome in which recurrent pneumonitis and eventual bronchiectasis, with or without atelectasis, are thought to occur as a result of compression of the right middle lobe bronchus by inflammatory nodes.

Figure 4 is the bronchogram of a right lung, lateral view, made with Dionosil Aqueous. The patient, a female of 63 years, was examined because of recurring profuse hemoptysis, and although the initial roentgen examination and bronchoscopy had been negative the bronchogram shows large bronchiectatic saccules in the anterior basal segment of the right lower lobe and also in the superior segment of the same lobe.

Figure 5 illustrates a case of so-called asthmatoid bronchitis in which Dionosil Oily was instilled for bronchography. There is a striking contrast between the normal-appearing upper lobe and the middle and lower lobes, where the "dead-tree effect" is quite evident, and there is some degree of broncho-stenosis of the right stem and lower lobe bronchi. We have seen no untoward sequelae of Dionosil instillation in cases such as this, but feel that, regardless of the con-

Fig. 4.—Bronchography with Dionosil Aqueous. Saccular bronchiectasis of superior and anterior basal segments of right lower lobe.

trast medium used, particular care should be used in bronchography in the presence of diffuse peripheral obstruction.

Naturally, one is anxious to be as certain as possible that the preparations of Dionosil are free of significant toxic effect, either local or systemic. As concerns the contrast substance, animal metabolism studies[2] have indicated that the propyliodone, following hydrolysis, is excreted by the kidney in the form of the sodium salt of 3:5 di-iodo-pyridone acetic acid. Since iodopyracet is excreted in this same form, and since much larger quantities of iodopyracet are given in a short time, by the intravenous route, for urography and other purposes, there seems to be no reason to fear renal or systemic toxic effect from this agent.

Special studies on rabbits, by Tomich et al,[2] employed both the aqueous and the oily preparations. This investigation was a well controlled one, and involved gross and microscopic examination of the lungs of animals sacrificed at intervals of 16 hours, 3 days, 5 days, 2 weeks and monthly up to 5 months after the instillation. In addition to microscopic examination for inflammatory changes at these intervals, special staining techniques were used to detect the presence of residual sodium carboxymethylcellulose or arachis oil. Small quantities of carboxymethylcellulose could be detected during the first three or four days following the instillation of the aqueous preparation, but in none of the animals could this substance be seen after the fifth day. Following instillation of Dionosil Oily, droplets of non-opaque oil were present in the bronchi for a similar period, but not longer.

We have previously[1] reviewed some of the literature describing effects of oily and aqueous preparations for bronchography on the lung. Felton,[5] in a recent study of 37 resected specimens of human lung, 23 to 295 days after instillation of Lipiodol, found residual oil in 23 instances, and in 6 of these (16 per cent of the entire group) non-specific granuloma of the foreign-body type was found surrounding the droplets of Lipiodol. Cummins and Silver,[6] on microscopic examination of 4 surgical specimens removed from 3 to 49 days following bronchography with Dionosil Oily, found droplets of oil in alveoli and alveolar walls, but in the specimen obtained 7 weeks following bronchography only occasional droplets were found, even in diseased areas. No granuloma formation was observed in these cases. Holden and Crone[7] report the microscopic examination of six surgical specimens removed from 5 to 19 days following bronchography with Dionosil Oily, in which no histologic changes attributable to the contrast medium, except for simple phagocytosis, could be demonstrated in either diseased or non-diseased areas.

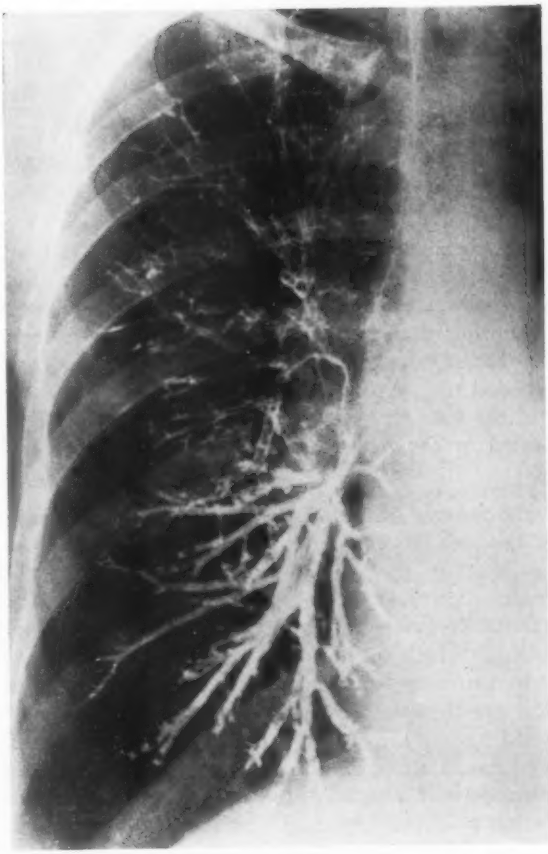

Fig. 5.—Bronchography with Dionosil Oily. Broncho-stenosis and "dead-tree effect" right middle and lower lobes in a case of "asthmatoid bronchitis."

In five patients of our own, whose surgical specimens were examined from one to eleven days following instillation of Dionosil Aqueous, the histologic changes in portions of the lung shown on bronchogram to have been well filled were thought to be of minor degree, the peri-bronchial cellular response consisting chiefly of lymphocytes, plasma cells and macrophages.

Clinically, Dionosil has been quite free of toxic effect. Transient temperature elevations have been reported[7, 8, 9] and occurrd in some of our cases. A review of the temperature charts of 57 patients who had been hospitalized at the time of Dionosil bronchography showed elevations of 100° F. or less in 7 cases (12 per cent), of 100° to 102° in 7 cases (12 per cent) and of over 102° in 4 cases (7 per cent). In only 4 instances did the elevation persist beyond 24 hours, and in only two cases was there any fever beyond 48 hours. Such febrile reactions, which occurred a little more frequently following use of Dionosil Aqueous than after Dionosil Oily, are also observed in a certain number of cases following bronchoscopy and iodized oil bronchography, and are not thought to be of any great importance. Don has advised the use of prophylatic antibiotics if bronchography is to be performed in the presence of appreciable degrees of bronchial infection.

In only three of the total series of 132 Dionosil bronchograms (87 with Dionosil Aqueous and 45 with Dionosil Oily) were there sequelae other than the temperature elevations detailed above. In two instances chest pain, not of pleural character, was observed beginning about 36 hours following the instillation of Dionosil. In one of these, in which the Aqueous preparation had been used, there was an accompanying temperature elevation of 100.6,° but findings on physical examination were negative. Both the pain and the fever had subsided by the third day, and a roentgenogram on the fourth day showed no abnormal densities. In the second case, in which the oily preparation had been used, the temperature rose to 103° on the third day, but pain and fever had both subsided by the fifth day. In this case also a roentgenogram on the 4th day had shown nothing to suggest pneumonitis, atelectasis or pleural reaction. In the third case, a transient pneumonitis was evident on x-ray two days following instillation of Dionosil Aqueous. Antibiotics were not given, but the abnormal density had cleared in an x-ray made five days later.

SUMMARY AND CONCLUSIONS

1. Observations on the properties and bronchographic characteristics of Dionosil are recorded. Dionosil Aqueous, an isotonic suspension of propyliodone incorporating sodium carboxymethylcel-

lulose as a viscosifying agent, lacks the irritant quality of aqueous media hitherto available. Although of lower viscosity than the iodized oils, alveolar filling of appreciable degree does not occur, so that the instillation and incidental fluoroscopic observation need not be hurried, as in the case of iodized oils. The bronchograms are characterized by uniform mucosal coating, and excellent demonstration of the smaller peripheral bronchi may be achieved with consistency. Elimination of the contrast substance is usually complete by the fourth day, with no residual opacities of the type seen following iodized oil instillation.

2. Dionosil Oily in general offers the same advantages as the aqueous preparation; its use requires somewhat less topical anesthesia, but there is a greater tendency for alveolar filling and elimination from the bronchial tree requires two or three days longer.

3. Local and systemic toxic effects of Dionosil appear to be of minor degree; experimental and clinical data are briefly reviewed.

4. Our current bronchographic technique is described, and illustrative bronchograms are presented.

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(Scientific papers of the American Broncho-Esophagological Association to be continued.)

Society Proceedings

CHICAGO LARYNGOLOGICAL AND OTOLOGICAL SOCIETY

Meeting of Monday, December 7, 1953

THE PRESIDENT, DR. ROLAND RUSSELL, IN THE CHAIR

The Otologist's Role In the Industrial Hearing Conservation Program

MEYER S. FOX

(Abstract)

Otologists who are interested in hearing conservation programs in industry may cooperate with and often supervise industrial nurses and physicians and safety personnel, and contribute their share toward the accomplishment of a sound hearing conservation program, the purposes of which are: 1) to conserve the hearing of workers; 2) to prevent unnecessary economic loss to employers and 3) to collect and evaluate research findings and data in order to increase theoretical knowledge and practical effectiveness in this field.

Because of his special training and clinical experience, the otologist can offer realistic advice on: 1) the tailoring of a practical program to meet the needs of a particular plant; 2) selection of a suitable room for conducting hearing tests; 3) selection of an audiometer and checking its performance; 4) instruction and guidance of plant personnel in conducting hearing tests: 5) evaluation of preemployment and periodic hearing tests; 6) placement of workers with impaired hearing; 7) selection, fitting and use of ear protective devices; 8) the susceptibility of individual workers to occupational hearing loss; 9) the detection of willful exaggeration of either hearing ability of hearing loss on the part of workers.

When the hearing conservation program is installed and begins to take effect, the average industrial concern will experience a pronounced decrease both in subjective complaints from workers and in the number of hearing loss claims filed with the Industrial Com-

mission. The otologist can participate in the medico-legal evaluation of such claims and differentiate between noise-induced hearing loss and losses attributable to other causes. He may be called upon to render expert opinions on such issues as the following:

At what level of sound intensity and over what period of exposure does hearing damage take place?

What was the status of the employee's hearing when he began work for a particular employer?

What tests should be used for assessing the hearing loss?

What formulae should be used to evaluate hearing test results in terms of percentage of disability?

Which of several different hearing test results obtained by several doctors on different days should be accepted as valid?

Are some workers more susceptible to noise-induced hearing loss than others?

How long after his removal from intensely noisy working conditions can a worker's deafness be judged to be permanent?

Often the known facts in a particular case allow only a partial or provisional answer to these questions. The need for research and the paths in which it should be directed are plain. Already, results of hearing studies coupled with medical and industrial histories have been obtained on thousands of workers in the Wisconsin area. Together with similar data collected in other states, these statistical studies are beginning to fill in the gaps in our knowledge and to make speculation about the facts of hearing loss in industry unnecessary. It is hoped that more otologists will interest themselves in the efforts of industry, labor groups and others to overcome the hearing loss hazard, and that through the continued cooperation of the various members of the hearing conservation team, the problem will be overcome.

DISCUSSION

DR. H. G. KOBRAK: We are indebted to Dr. Fox for this interesting discussion of the problems of industrial noise. We are more indebted to him because of the decision he made a number of years ago to study the problem in detail. Under considerable difficulty and with great personal sacrifice he started an active audiometric study in industry and thus provided the otological profession with much needed data for further studies. He has made it clear that we are still in the initial phase of the problem. The industrial and

military causes of ear damage by excessive stimulation are still growing and the legal problems are attaining an increased momentum.

The otologist has two problems to solve. The practicing otologist is being asked to examine and to interpret the hearing of the individual patient and, the otological profession must provide answers to the generalized questions which Dr. Fox has named.

So far as examination of the patient is concerned, much discussion has been centered on the question of pure tone audiometry versus speech audiometry. The scope of usefulness of each method has not always been respected fully. The pure tone audiogram is an excellent diagnostic method. It permits the diagnosis of hearing impairment, it indicates the site of the lesion (the conducting mechanism in the end organ or retrolabyrinthine). But it is a completely different problem to assess the quantity of damage for medico-legal purposes. The patient who demands compensation is not suing because he has a pathologic, absolute pure tone threshold audiogram; he is concerned because he cannot understand conversation. Would it not be more direct to test the perception of the spoken word? Pure tone audiometry is not easily translated and evaluated into speech performance. We have several formulas to assess and to interpret the curves (A.M.A., 0.8, Fowler, Kinney, Veterans' Administration, etc.). But it would seem a better investment to direct our efforts to the development of speech audiometry rather than to designing new calculations and arguing about the interpretations of the pure tone audiogram.

As to the general questions which the otological profession must answer, many otologists have had the experience in court proceedings of having questions such as "What is a safe noise level?" "How long may an exposure be tolerated before it becomes damaging?" posed to them. One cannot assess the damaging effect of a noise level without considering the time of exposure and the length of the recovery period. As biologists, we must insist that legal minds do not succeed in tying a straitjacket around biologic problems.

A word with regard to predetermination of susceptibility of some workers to excessive noise. It was the opinion of otologists at the International Congress in 1949 that fatiguing tests of short duration as recommended by Peyser, Kriml, Wilson or Theilgand do not permit differentiation between resistant and hypersensitive ears. It would seem, therefore, that it is not a wise procedure for the otologist to grade applicants. He should not advise management to abstain from hiring a man on the grounds of his performance in the pre-employment fatiguing test. However, prevention of

noise damage is possible if the applicant has a pre-employment audiogram and repeated audiometric examinations thereafter; the susceptible workman with early damage and poor recovery powers can be weeded out. He can be detected before serious permanent damage occurs in his cochlea. Inasmuch as there is no treatment known for cochlar pathology once it has occurred, the importance of early diagnosis is all important. The value of audiometric examinations, as pre-employment and as follow-up studies, must be stressed. The worker with above average noise sensitivity can be detected before his training and experience become so advanced that management may be unwilling to transfer him to a different job. This is the positive answer otology can give to industry.

No single man, no single group or profession can study fully or solve the problem of acoustic trauma. Teamwork is essential. Two years ago the University of Michigan organized an intensive study course for all those interested in the industrial noise problem. For three days an intensive study and exchange of opinions brought out all important aspects. Many questions remained unanswered, and many fields for further study were pointed out, among which were the need for facts, for field work. This is the great value of Dr. Fox's work. By giving us the figures and relating his experience in the field, he has provided the basis for evaluation and planning. His work is an important cog in the machinery which has been set up to fight the dangers and the damages of acoustic trauma.

Dr. Alfred Lewy: Dr. Fox has presented a subject that should be of great interest to the otological profession as well as to industry, and undoubtedly will be to insurance circles. It has attracted much interest in the Scandinavian literature, and even little Finland has a new law since 1953 which requires pre-occupation examination of the hearing of workers in noisy industries and periodic examinations thereafter, and containing clauses concerning the structure and mechanical control of noise in factories, shipyards, etc. It is quite probable that with Workmen's Compensation laws in this country covering damage to the hearing, the insurance companies will see to it that Dr. Fox's suggestions are considered.

In the State of Illinois only total deafness is compensible—an unfair situation. Moreover, arbitrators on the Industrial Board are not agreed as to what constitutes "total deafness;" whether it means total for industrial purposes, insofar as it limits a man's chances for a job and his safety on it, or total in the absolute sense. So far as I know the Supreme Court has not yet ruled on such a case.

Wide Field Laryngectomy: Motion Picture

WATER P. WORK

(Abstract)

This is a motion picture illustrating the detailed techniques in wide field laryngectomy. The approach to the surgery of this area of the neck is stressed according to facial planes and pertinent anatomic structures. These are worked out on fresh cadaver material and the motion picture illustrates the technique and procedure of dissection. In addition, a collar type of incision used by the author is shown. Two sections of the picture show the operation as performed on a fresh cadaver, and the actual operating room procedure on the living. The film is accompanied by an explanatory sound track.

DISCUSSION

DR. BURTON J. SOBOROFF: The movie which we have seen shows a technique of wide field laryngectomy easily applicable in all those cases in which laryngectomy is indicated. We need not discuss the indications and contraindications for laryngectomy since these have been so well presented on other occasions.

However, all those who have done this operative procedure have had cases in which there has been local recurrence which might have been prevented by wide resection. These recurrences may develop in the region of the thyro-hyoid membrane, above the tracheal stoma, or about the tracheal stoma and in the tracheal mucosa. The procedure of wide field laryngectomy extends the operation from the tracheal area to the level of the base of the tongue, including in dissection the strap muscles and the hyoid bone. Removal of the hyoid bone provides for adequate removal of the entire pre-epiglottic space into which the tumor can so readily extend anteriorly from the larynx. Removal of all the strap muscles in single block dissection is done in an attempt to remove any tumor which may have extended anteriorly from the larynx into these tissues or through a prelaryngeal node.

Resection of the entire cricoid together with one or two tracheal rings provides a wide field of safety below the lesion in the event of subglottic extension which, in many instances, cannot be seen accurately before surgery. Dr. Work has not presented any additional wider indications for total laryngectomy, but has tried to emphasize that in those cases in which laryngectomy is indicated, a

wide field procedure (such as the movie demonstrates) should be done.

Dr. Maurice F. Snitman: I had the opportunity to preview both films and it was quite obvious that the operative procedure on the cadaver was much more instructive and understandable. Color production on film of surgical procedures on the neck of the living are, as a rule, unsatisfactory, and the same holds true for still and movie reproductions.

It would appear that the term "wide field" was coined for the purpose of drawing attention to a procedure that is contrary to narrow field laryngectomy. In this presentation the author does meet an important requirement of neck surgery, that is, adequate exposure and dissection. This basic feature I heartily commend, although I do not favor a few of the technical elements. I am especially critical of the term "fascia" which is so frequently repeated in the description of the procedure. I must emphatically state that true fascia of the neck does not exist. What is alluded to is a false impression of a fascial layer, produced by the condensation (as a result of the surgical dissection) of the loose connective tissue of the neck.

Dr. L. Benno Bernheimer: It was a privilege to see Dr. Work's movie. I am sure that his indication for the procedure is the presence of extrinsic disease. I am still of the opinion that intrinsic non-infiltrating carcinoma responds as well to irradiation as to surgery but, on the other hand, for the type of disease that I assume the author is treating, irradiation would be merely palliative. Radical neck surgery is not new. Radical neck dissection and laryngectomy with wide exposures were performed many years ago, but the mortality was so high that such procedures were abandoned. The advent of chemotherapy and the antibiotics has altered this picture so that today almost nothing is considered anatomically inoperable.

Dr. Irwin D. Horwitz: The procedure just demonstrated was for carcinoma of the extrinsic larynx or hypopharynx. Any criticism of this should be based on the fact that the operation was not extensive enough, not on the esthetic viewpoint that it is too mutilating. Tumors of this area metastasize early and most radiologists will concede that they cannot successfully treat metastatic tumors. The best results claimed are between 10 and 12 per cent for five year cure rates. The suggestion of Dr. Bernheimer that x-ray and irradiation be used does not follow the dictates of practical therapy. A treatment consisting of one-half surgery and one-half irradiation adds up to a therapeutic zero. In past years wide ex-

tensive surgery has offered the promise of a better salvage ratio and, equally improvement, an earlier rehabilitation.

Inner Ear Deafness Due To Measles

JOHN R. LINDSAY

(Abstract)

Loss of hearing due to measles has commonly occurred in two ways; the result of bacterial middle ear infection, and an acoustic neuritis due to the measles virus. Antibiotics have been effective in controlling the middle ear infections but not the acoustic neuritis or inner ear deafness due to the measles virus.

Several surveys have indicated that inner ear deafness due to measles accounts for three to five per cent of acquired deaf-mutism. Unilateral deafness and bilateral hearing impairment are also reported to be not infrequent.

Reports on the pathology of uncomplicated acoustic neuritis due to the measles virus have been extremely rare.

The inner ear changes in a child who died of complicating myocarditis several weeks following measles are presented. Both ears showed changes in the organ of Corti, tectorial membrane and stria vascularis, more marked in the basal turn. There was nerve and ganglion degeneration in the basal turn. The utricles, saccules and cristae of the semicircular canals were also involved. Lesions were evident in the stria vascularis and utricle which may represent the basic pathologic lesions due to the measles virus.

DISCUSSION

DR. ELMER W. HAGENS: In 1930 several of us reported on the examination of more than 5,000 children in schools for the deaf. Of this group, about 2,000 had acquired deafness; 172 children, or 8.5 per cent, had become deaf following measles. Considering the measles cases alone, we found that 51 had an associated otitis media, while 121 had become deaf without otitis media. Both groups were divided into total and partial deafness and the vestibular reactions were recorded on all. As would be expected, the cases of total deafness without a history of otitis media, showed complete loss of vestibular reactions in 50 per cent. On the other hand, in total deafness associated with otitis media, 30 per cent had no vestibular re-

actions. The cases of partial deafness had a much lower percentage of cases without vestibular reaction. In the report we stated that it could be assumed that a toxic neuritis was no doubt responsible for the severe deafness in the two groups. The lack of vestibular response in many of these children also supported this view.

The child, whom Dr. Lindsay referred to from a previous article of mine, was 14 years of age and had developed measles one year before her death. Knowing her family doctor I was able to determine that she had been practically totally deaf for that year. Death occurred following a new respiratory infection with intracranial complications. I was able to obtain only the right temporal bone as the pathologist retained the other side.

Study of the microscopic sections showed no evidence of labyrinthitis, but there was complete absence of the organ of Corti, and a considerable destruction of the vestibular end-organs. The spiral ganglion cells were destroyed in great part while Scarpa's ganglion cells were fairly well preserved. I believe this case falls into the category discussed by Dr. Lindsay, as there was no labyrinthitis to obscure the picture. Such reports as Dr. Lindsay's will help to clarify what happens to the ear in cases of toxic neuritis.

Meeting of Monday, January 4, 1954

THE PRESIDENT, DR. ROLAND RUSSELL, IN THE CHAIR

The Management of Ménière's Syndrome

FRANK D. LATHROP

(Abstract)

A universally satisfactory method of managing patients afflicted with Ménière's syndrome apparently has failed to be realized even though the symptomatology and pathology of this syndrome are well established. This is attested to by the numerous and variable forms of therapy for this malady that have appeared in the literature during the past decade. It is not my purpose to discuss the pros and cons of these various forms of treatment since I intend to offer for consideration a program of management for Ménière's syndrome that has proved satisfactory in my hands.

In order for my method of treatment to be effective it is necessary that the correct diagnosis be established. It should be recognized that the triad of symptoms characterizing Ménière's syndrome (deafness, tinnitus and vertigo) may be the manifestation of many diseases. The diagnosis of Ménière's disease should be made only when no other explanation can be found for these symptoms. Patients with typical Ménière's syndrome complain of tinnitus and severe attacks of labyrinthine vertigo associated with bilateral nerve deafness which is usually more profound in one ear. The diagnosis cannot be substantiated on the basis of a single, isolated attack of labyrinthine vertigo even though it may be accompanied by deafness and tinnitus since, by definition, the vertiginous attacks must be recurrent. The hearing early in the course of the disease may fluctuate to a considerable degree, with the lower frequencies most affected. As the disease progresses, the hearing loss becomes more profound, fluctuates little, and higher frequencies are most affected.

Approximately 85 per cent of the patients whom I diagnose as having Ménière's syndrome respond satisfactorily to the following medical regimen. This consists of a diet low in sodium content and the administration of ammonium chloride to facilitate the elimination of unnecessary sodium from the body. The patient is instructed concerning a diet which permits him to eat most of the food he desires as long as it is not salted at the table. Articles of food that are cured with salt, such as ham and bacon, are prohibited as are also flavoring agents such as catsup, mustard, Worcestershire sauce, and so forth, since they contain excessive quantities of salt for the dietary purpose. Pepper, olive oil and vinegar may be utilized as desired to flavor the food. Ordinary bread and butter in normal quantities may be used. This diet can be followed equally well in the home or the restaurant and thus eliminates to a large degree the impracticability of following a strict dietary regimen when the patient is away from home.

Ammonium chloride is utilized as an enteric coated tablet. The initial dosage is two gms three times a day with meals for three days, omitted for two days and repeated at these intervals for an indefinite period. The patient is instructed to take the tablets spaced throughout his meal. If he is in the habit of eating a small breakfast, two tablets may be taken then and five tablets with dinner and supper or, if both breakfast and lunch are small meals, two tablets are taken with each of these meals, four with supper and two tablets between breakfast and lunch, and lunch and supper. If this manner of administration is followed the incidence of gastric irritation is reduced to a minimum.

The success of this form of treatment is augmented if the patient is made aware of the nature of his illness and thoroughly understands the rationale of the medical regimen, as only through this knowledge can he actively participate in the management of the therapy, just as does the diabetic. He must be seen at periodic intervals in order to observe his progress, to make necessary alterations and additions to the medical regimen, and to strengthen the relationship between the patient and the physician, so that questions may be answered reasonably and assurance given that something else can be done to relieve the dizziness if this treatment fails. Since many patients with Ménière's syndrome are either in the older age group, with additional symptoms secondary to arteriosclerosis, or are nervous, nicotinic acid, mild sedation or both are often helpful in further effecting their rehabilitation.

In the event that the patient fails to obtain relief from the paroxysmal attacks of vertigo from any form of medical therapy that may be employed, recourse must be made to some form of surgical procedure. For this purpose I have found the Cawthorne operation most satisfactory. This consists of sufficient removal of the cellular structure of the mastoid process to permit avulsion of the membranous semicircular canal through a small fistula created in the bony horizontal semicircular canal. This is a simple procedure as compared to intracranial section of the eighth cranial nerve and, in my opinion, is more satisfactory in effecting rehabilitation of the patient. It should be emphasized, however, that if the medical management of Ménière's syndrome is assiduously carried out, the necessity for surgical intervention will be infrequent.

DISCUSSION

DR. JOHN BALLENGER: I was surprised that Dr. Lathrop did not make more mention of the use of autonomic blocking agents, particularly of the cholinergic nerves. I assume he employed Dramamine® for that purpose, but there are others such as Banthine® or tetraethyl ammonium which would seem to be more efficient over a longer period; 50 mgm of Banthine® three times a day, in my more limited experience, has been quite helpful.

I should also like to inquire about the fluid intake. At one point he suggested a high fluid intake if there was a reaction to the use of ammonium chloride. Except for this, it would seem to me that a low fluid intake would be better advice to the patient.

DR. ALFRED LEWY: We are indebted to Dr. Lathrop for a most detailed description of Meniere's disease, to which I cannot

add much. I would like to suggest that the audiogram would be effective here in helping to indicate in which ear surgery should be done, in case surgery is contemplated. An erratic or a changeable audiogram would make one suspicious of Ménière's disease, as would also a patient who reacts more violently to a caloric test than is usual; in that case I would suspect psychoneurosis. Of course the patient with Ménière's disease might also develop psychoneurosis. The old treatment with pilocarpine is probably effective by dehydration. I have used pilocarpine before any other definitive treatment was known, but the success of that requires hospitalization.

I would like to call attention to a drug which was not mentioned by the essayist, that is, pyridoxine, B_6, and to ask what his experience has been with this. In 1947 Dr. Fox and I published a report on some 87 cases of vertigo, of which 17 disappeared from our care and were considered failures. Of the 87 cases, 47 were diagnosed by us as Ménière's disease, the others were all vertigo of unknown etiology. Of the latter group many were helped by the use of pyridoxine, and 75 per cent of those diagnosed as Ménière's disease were benefited. Since then I have definitely increased the dosage; we formerly gave 50 mgm three times a day. We now give 50 mgm ordinarily, and in more severe cases 100 mgm. In the very severe cases intramuscular or intravenous injections are given.

I do not know the pharmacology of pyridoxine. It has been used for the nausea of pregnancy and does not always work there. It has also been used successfully for treatment of agranulocytosis, and some neurologists have reported it effective in relieving the spastic symptoms of multiple sclerosis. I do not know how it works and wish someone would tell me. It is not very successful in motion sickness; dramamine is probably better.

Dr. John R. Lindsay: I should like to congratulate Dr. Lathrop on his very careful and clear description of the symptoms of Ménière's disease and the attention he pays to making an accurate diagnosis. It is very important that this be done, since even after many years in which it has been discussed a great deal, there is still some confusion about what constitutes true Ménière's disease.

One point that is important in the general management of the disease (and which is exemplified by the detail with which Dr. Lathrop has described his medical management) is the care taken to regulate the patient's daily life in all its aspects. Whether it is mainly the psychic effect of his knowledge that you are taking a great deal of interest in his case I am not sure, but I suspect that the psychic aspect has much to do with it.

I agree with Dr. Lathrop that there is no point in using coagulation in the labyrinth. I have had no accidents with it but I have seen one case of total facial paralysis following coagulation. I have also seen one case recently which, following the Cawthorne operation, had a recurrence. There were repeated recurrences, and in that case I opened both the horizontal and the superior semicircular canals, opened the vestibule widely and destroyed its contents. I see no reason why that should not be done in the first place. Rather than just the horizontal canal, why not do a more thorough destructive job on the contents of the vestibule?

Dr. Sherman Shapiro: Our distinguished speaker has given an excellent summary of the subject, and I might say that the drugs he mentioned, ammonium chloride and nicotinic acid, are precisely those upon which I have relied for a good many years. There is one point I would like to add from the standpoint of diagnosis, and that involves the use of something of which I believe Dr. Lindsay and I are perhaps the chief protagonists in this vicinity, namely, the Frenzel glasses. In most cases of frank Ménière's disease, nystagmus can be seen quite readily, but after the acute attack is over many patients may feel pretty well; however, while nothing is seen by the unaided eye, when the glasses are put on they exhibit a horizontal nystagmus which of course enables the physician to say at once that the condition is not psychic. This, also by laws of labyrinthine irritation and destruction, sometimes helps to differentiate between the two sides when this is in doubt. Many of these people have just a slight dizziness, as Dr. Lathrop mentioned, and it is a satisfaction to know that they are not just imagining it.

I should like to ask Dr. Lathrop what his experience has been with potassium instead of ammonium chloride.

Dr. Robert Lewy: I should like to ask Dr. Lathrop how he differentiates with relative certainty the fact that he is not dealing with a supravestibular type of vertigo. Certainly we have all had to deal with this from time to time, and any destructive operation on the vestibule under those circumstances would have a greater tendency in the direction of failure, I am sure. Does he use the recruitment test among other things in helping to establish the diagnosis? Does he make an allergic evaluation of the patient? I have had some good results in finding some specific allergens in the form of food which would precipitate a Ménière's attack, and removal of the offending allergen of course solves the problem.

In terms of surgical intervention, my colleagues and I have been working for seven years in a large public institution which receives

difficult cases from all over the United States. We have not had one case which, by our standards and in our opinion, has required a destructive operation of the labyrinth. It has always puzzled me as to whether our standards are different, or whether by virtue of reputation or for some other reason, those cases get into other hands where surgery is necessary. Prior to the work of Passe and Seymour, in which they cut the thoracic anterior gray rami (first they took out the stellate ganglion, then later the anterior gray rami in the upper thoracic region) the only surgery done was one or another type of destructive surgery. Based upon their work Hoagland proceeded to do repeated stellate ganglion block and claims to have had some very satisfactory results and to have avoided surgery. I have not had much experience with it, but it would seem that if he is right, a patient should be subjected to a trial repeated stellate ganglion block, and have a destructive operation on the cochlea only if this fails.

Dr. Elio Fornatto: I should like to mention some work that has been done in Italy on surgical procedures for the partial destruction of the labyrinth with suppression of the vestibular function without deterioration of the cochlear function. As we know, the Cawthorne operation involves complete suppression of the hearing function in the ear operated upon. Two surgical procedures have been studied in Italy. At the University of Turin a new method has been carried out in animals and in man. This consists of a fenestration operation with introduction of fibrin sponge in the semicircular canal in order to determine the formation of fibrotic tissue. The histology of successive changes has been studied. Animals show a normal cochlear function after destruction of the vestibular labyrinth. In man, however, the hearing function deteriorates until there is complete loss. Therefore the value of this procedure will be seen only in the future. At the University of Padua, Professor Arslan destroys the function of the vestibular apparatus by direct application of a bundle high-frequency sound waves to a semicircular canal following an extensive mastoidectomy. A special apparatus is employed and particular care is needed to avoid facial palsy. In all cases the hearing remained the same as before the operation. The results have been controlled several months after operation.

Dr. Henry B. Perlman: In the hope of obtaining some information about the pathogenesis of this disease and to evaluate the commonly employed low salt diet regimen, we recently studied a group of patients with active Ménière's disease in the hospital with the co-operation of Dr. Goldinger of the Medical Department.

Ordinarily it is very difficult to change the body electrolyte balance by dietary means. In these hospitalized patients we were able to produce a small but measurable reduction in the serum sodium. This was accomplished after a week or two on a 300 mgm sodium diet with the administration of thiomerin and of ammonium chloride and sometimes intravenous aminophyllin. These patients had active Ménière's disease as manifested by measurable fluctuating hearing loss and recurring attacks of vertigo. Their clinical state was not changed during the period when there was a measurable reduction in this serum sodium. Auditory threshold curves continued to fluctuate as before and two patients had typical acute violent attacks of vestibular vertigo and nystagmus.

We then did a converse experiment with these patients—deliberately raising their serum sodium. This was accomplished by giving them desoxycorticosterone, additional sodium chloride in the diet and restricting their fluid intake. A measurable increase in the serum sodium was obtained. Strangely enough, the patients did not get worse under the regimen. Their hearing did not deteriorate nor did they experience attacks of vertigo. Instead, in two patients there was a return of the previously reduced auditory function to a practically normal level. It is of interest that despite all our investigations and astute clinical observations, the pathogenesis of this disease is obscure.

Dr. Frank D. Lathrop (closing): I do not know the answer to this particular problem. Certainly it is very difficult to demonstrate any particular changes so far as electrolyte balance is concerned, but the fact remains that the program I have offered to you will give good results if it is followed as assiduously as I suggest.

This brings up a very delicate question. Are these patients benefited becaused of the medical regimen or because they have confidence in the doctor? I do not know, but it makes no difference to me since the patient is happy and is able to work, which he could not do before. You cannot just give these patients something to do, you must follow them along. Sometimes I find after I have seen them two or three times that the diagnosis of Ménière's syndrome is erroneous, and I change the program of treatment. But the point I wish to emphasize is that the patient cannot be treated offhandedly. He must be made to realize that he has someone to whom to turn in case he has trouble and that his physician is willing to help when he is in trouble.

I learned long ago that if I desired to become proficient in the management of a disease it was necessary for me to learn how to

handle all the details of one or two forms of therapy. I do not believe there is a man alive who can do neurosurgery, otolaryngology, ophthalmology and general surgery as well as he can an individual specialty.

I think the use of Banthine,® which Dr. Ballenger mentioned, might be effective. I have never used it because I have found effective measures of relief for my patients without the use of banthine. It may be a good drug, but I have learned how to use others and I stick to them.

With respect to the management of an acute attack, and this will also answer Dr. Lewy's question about stellate blocks, I have found that in an acute attack a stellate block with 1 per cent procaine apparently does relieve the dizziness. I do not believe, however, that repeated blocks of the stellate ganglion constitute a rational form of management for Ménière's disease. I have yet to see a case of a cerebellar lesion or supratentorial lesion which has produced dizziness that resembles that of Ménière's syndrome. Again I wish to emphasize that between the attacks of vertigo the patient may be entirely asymptomatic except for tinnitus and deafness, but the individual who has a brain tumor and who has vertigo is never free from a sensation of unsteadiness.

So far as the fenestration operation is concerned or the plugging of the fenestrated horizontal semicircular canal with gelfoam, essentially the same thing was employed some years ago by Dr. Lindsay without permanent beneficial results being obtained.

The point Dr. Shapiro brought out with respect to Frenzel glasses is very good. Strangely enough an occasional patient will not respond to ammonium chloride but will respond to potassium chloride and a low salt diet.

With respect to fluid intake, at no time have I said that the patient should have a high fluid intake. I ask him to continue his normal fluid intake. Many patients automatically cut down on fluid intake when they start a salt free diet. Such patients frequently become constipated and I ask them to increase the fluid intake but not to make it a high fluid intake.

Dr. Lindsay asked whether I used Streptomycin.® I have not, for the reason, again, that I have been able to rehabilitate the majority of my patients with the therapy I have described. Thus far I have had no failures from surgical intervention.

Some Problems In Antibiotic Therapy

HARRY F. DOWLING

(Abstract)

The antibiotic-resistant strains of bacteria which are a problem in otolaryngology are almost entirely staphylococci. These, however, constitute a problem of ever-increasing importance. We have found that resistant strains may appear as a result of 1) treatment of a patient with a staphylococcic infection; 2) spread from a patient who has been so treated or; 3) spread from contacts of patients who have been treated with the antibiotic, specifically hospital personnel. The emergence of resistant strains may be delayed by the use of combinations of antibiotics in some instances, but can be prevented only by rapid termination of the infection and discontinuance of the administration of the antibiotic. The spread of resistant strains can be prevented by proper isolation technique and by the development, in new hosts, of resistance against infection.

The wholesale use of antibiotics for upper respiratory infections is to be condemned because it increases the frequency of hypersensitivity reactions and accelerates the emergence of resistant strains.

Among the new drugs, Erythromycin®and Carbomycin® are of some value for infections caused by gram-positive cocci, while tetracycline (Achromycin®) is an analogue of Aureomycin® and Terramycin® which gives fewer gastrointestinal reactions, is more stable and penetrates into the spinal fluid more readily than Aureomycin® or Terramycin.®

DISCUSSION

DR. ROBERT HENNER: What is your feeling about the routine use of penicillin in preoperative cases where there is no infection?

DR. SHERMAN SHAPIRO: Do you know how the development of resistant strains is affected by the combined use of such antibiotics as penicillin with the sulfonamides?

DR. ROLAND RUSSELL: What about the local use of antibiotics?

DR. STANTON A. FRIEDBERG: I wonder if you would tell us of any experiences you have had in which antibiotics, through a toxic effect, were able to mimic a severe infection and thus be misleading.

DR. SAMUEL J. PEARLMAN: What do you think of combinations of antibiotics and antihistaminics?

Dr. Harry F. Dowling (closing): With regard to the prophylactic use of penicillin preoperatively, I feel that there should be some good controlled series before such measures are carried out. It is strange that there is little in the literature concerning such studies on the prophylactic use of penicillin. One report made by a thoracic surgeon showed that the incidence of empyema was lower in patients who received penicillin routinely before operations on the lung. However, until we know more about it I feel that antibiotics should be used prophylactically only when the operation is performed in an infected area or when there is a threat of infection. If that rule were followed, we would not have so many patients becoming sensitive to the antibiotics.

There is no evidence that a combination of penicillin and one of the sulfonamides will delay development of resistant strains. The sulfonamides are so much less active than the antibiotics that they do not add much. The percentage of resistant strains would be about the same. That is particularly true of the staphylococcus.

There is little reason for the local use of penicillin or any other antibiotic. Certainly, in my opinion, troches or lozenges should never be used. They give a concentration on the surface of the mucous membrane of the mouth, but that is not where the bacteria are. The use of the antibiotics in the sinuses is another matter, because the material remains there for a certain length of time and can penetrate the membranes. I believe that penicillin should be employed only occasionally on the skin (although it is being used frequently) and again we may get sensitivity reactions from such applications.

Sensitivity reactions can mimic infection, particularly in the acute attacks with fever, skin reactions, joint pains and swelling. A careful history can usually elicit the cause, and the antibiotics can be stopped and the reaction controlled.

I prefer to reserve the use of antihistaminics until the reaction is noted, because of their masking qualities. In a severe reaction they have little effect and will not prevent an acute anaphylactic attack.

Abstracts of Current Articles

EAR

Late Results of Cases of Conservative Atticomastoidectomy Without a Meatal Flap.

Oka, F.: The Jour. of the Otorhinolaryng. Soc. of Japan 56:615, 1953.

The author summarizes his observation on fifteen cases after two years, on an average, since the operation. In all cases the wound had completely healed. The findings were: 1) unchanged in ten cases, 2) relapsed in two cases, 3) crust formation at the perforation of the drumhead in one case, 4) somewhat moist at the postero-superior part of the drumhead in one case, 5) polyp formation at the perforation in one case. Cases three, four and five were re-treated and all were cured within five days. Hearing was found unchanged in eleven cases, improved in one case and slightly depressed in three cases. The external aural canals were unchanged and normal in nine cases, slightly retracted at the postero-superior part in five cases and greatly retracted in one. In one case web formation at the external aural canal was observed.

HARA.

An Experimental Study of Pathology Changes in the Ear Caused by Galvanization.

Obata, T.: The Jour. of the Otorhinolaryng. Soc. of Japan 56:619-629, 1953.

Direct current of various strengths (7 to 30 mA) and various duration (10 to 60 sec.) was sent into a guinea pig's ear via the electrodes inserted into each external ear canal.

Decapitation or intravitam fixation was performed while the current was still on, and the auditory organ was histologically examined to establish the effect of the more or less prolonged galvanization.

During the galvanization, nystagmus, trembling movement or sustained deviation of the eyeball were observed. On histological investigation traumatic changes prevailed over the whole range of the auditory organ, on the cathodic side rather than the anodic. Changes

both in sensory and in supporting cells of cristea and especially of maculae, and in ganglion cells, were on each side quite characteristic.

Galvanization effect on the anodic side was first manifest as nuclear pyknosis in sensory cells. Stronger current showed first in edematous swelling of the cytoplasm, then in swelling of the nucleus toward the surface of the neuroepithelium along with the swelling of the nucleus, and further pyknosis and displacement of the nucleus toward the surface of the neuroepithelium along with the swelling of the cytoplasm.

Disturbed arrangement and constriction were the first signs detected in supporting cells as the result of the galvanization, occurring with the swelling of sensory cells. On the cathodic side similarly a stronger effect was observed, i.e. disorder in sensory cells, the pyknosis of their nuclei and disturbance in supporting cells. These effects appeared in an intensified degree as the strength or the duration of the constant current used in the experiment increased.

HARA.

Pneumatization of the Mastoid Process in Relation to Occupational Deafness.

Dohi, K.: The Jour. of the Otorhinolaryng. Soc. of Japan 56:537 (July) 1953.

An observation on the relation between the pneumatization of the mastoid process and the loss of hearing was made on 100 laborers working in a noisy environment (exceeding that of 90 phones) over a period of years in a shipyard.

In a group of 68 laborers who had been employed from 10 to 15 years, it was observed that those with well-developed pneumatization had a slighter loss of hearing than those having undeveloped pneumatization. In a group of 32 laborers who had been employed over 30 years this relationship was not recognized. The same relationship between the pneumatization and deafness was observed between the ears. Therefore air cells of the mastoid process obviously have a preventive influence against the loss of hearing due to strong, persistent noises.

HARA.

Functional and Histological Findings after Obliteration of the Periotic Duct and Endolymphatic Sac in Sound Conditioned Cats.

Schuknecht, Harold F., and Kimura, Robert S.: The Laryngoscope 63:1170 (Dec.) 1953.

This study describes the effect on hearing and inner ear morphology, of obliterating the periotic duct and endolymphatic sac. Unilateral destruction was performed on seven healthy adult cats by introducing a probe into the labyrinth through the round window membrane. The animals were then trained to respond to pure tone auditory stimuli and audiogram were determined using the continued avoidance response as an indicator of hearing. Beginning three weeks after each operation, tests of hearing were made at intervals of three to four weeks. The observation periods varied from one and one-half to seven months and the animals were then sacrificed and the inner ears serially sectioned and stained with hemotoxylen and eosin. The organ of Corti and the spiral ganglion were graphically reconstructed for each ear.

Destruction of the endolymphatic sac failed to create cochlear dysfunction or histological changes in the membranous labyrinth. Although surgical blockage of the periotic duct was associated with a moderate rise in Reissner's membrane in two ears, the evidence from this work is not sufficiently clear-cut to support the theory that this blockage causes dilatation of the endolymphatic system. In order to obtain more information on this subject, further studies were begun.

SENTURIA.

NOSE

Transpalatal Intervention in Congenital Atresia of the Choana. Case Report.

Xirau, J.: Rev. Cubana Oto-rino-laringol. 2:8:177, 1953.

According to embryological studies of congenital atresia of the choana, this rare condition is due to persistence of the bucconasal membrane, to secondary excrescences, or to anomalies of the internal wall of the sphenoid process. The surgical intervention most commonly employed, by the endonasal route, is sometimes unsuccessful because partial or complete closure of the operative opening may ensue in spite of tubes inserted to prevent the stricture, or subsequent dilatation may occur over a long period. Furthermore, this technique affords little or no visibility of the operative site. It is impracticable in the case of small children. When it is employed, it should be preceded by submucous resection of the septum.

The transpalatal access affords excellent visibility, and does not necessitate tubes or tampons.

A case is cited of chronic suppurative otitis media of the right ear, in a nine year old child, complicated by hypertrophy of the tonsils, mucous secretion in the left nasal fossa, small adenoids, and obstruction of the left posterior nares by a pearly, slightly umbilicated septum which rendered breathing difficult.

The Owens technique, modified by Ruddy, which was used in this case, is as follows: Under endotracheal anesthesia by means of a catheter introduced into the normal side of the nose, with the patient in Rose's position, a semicircular incision is made in the palatal arch, running from the second molar, back of the palatal veins, then forward across the palate, back of Scarpa's foramen and to the second molar of the opposite side. The palatal flap, including the palatal blood vessels is raised with a periosteotome, as far as the posterior border of the hard palate. An incision is then made in the midline, where the palatal mucosa is thin and adherent to the bone, to expose the nasopharynx. A hollow chisel or rongeur is used to incise the bone in the vicinity of the obstruction, which in this case was osteomembranous. A simple membrane can be readily removed but if the obstruction is a bony plate, the incision is made anterior to the margin of the bone, always toward the normal side. A rongeur is employed to extirpate the bone or osteomembrane. The vomer is exposed by incision of the mucoperichondrium of the posterior margin of the nasal septum. The mucoperichondrium is then detached on both sides of the obstruction. It is sometimes necessary to resect the septum also, to ensure an adequate opening into the posterior nares. A flap of mucosa from the opposite side of the septum is placed over the operative surface, at the site of the bone resection, and is sutured with chromic catgut No. 5-0. The palatal flap is replaced and sutured with silk No. 3-0. The sutures are removed on the fourth or fifth day. The patient is dismissed on the seventh day. In the author's case, examination six months after operation showed that the choanal opening was patent and adequate.

HIGBEE.

Bacteriological Study of Chronic Sinusitis.

Nakamura, M.: The Jour. of the Otorhinolaryng. Soc. of Japan 56:511-520, 1953.

Nakamura isolated 34 strains of 12 species of bacteria from 21 cases of chronic sinusitis of a year's duration or longer, and tested them on hemotoxin and plasma-coagulase in order to evaluate the virulence. He further followed the formation of antibody in sera

of the patients by means of agglutination tests. Also their susceptibility to penicillin, colistin and the sulfonamides was examined. The results are summarized as follows:

1. There are many etiological factors besides bacteria for the development of chronic sinusitis because the relationship between the virulence of bacteria and the severity of symptoms is not clear-cut, nor is the formation of the antibody manifest.

2. Sensitivity test of bacteria recovered from sinuses showed well against penicillin, colistin and sulfonamide. But, on clinical application these sinuses failed to respond to these antibiotics and sulfonamides, indicating that there are other factors than bacteria for perpetuating the chronicity of sinusitis.

HARA.

LARYNX

Bilateral Laryngeal Granuloma Following Intubation In Gas Anesthesia.

Munyo, J. C.: Rev. Cubana Oto-rino-laringol. 23:25, 1953.

The patient, a woman forty-eight years of age, had noted a persistent and progressive hoarseness for a month and a half. She was in good general health, and had not had vocal disturbances in the past. Two months previously she had undergone abdominal surgery under general anesthesia administered by intubation. The anesthesia had lasted for an hour and a half.

Indirect laryngoscopy revealed two polypoid tumors. The larger one was situated in the posterior portion of the left vocal cord. It was sessile and about one cm in diameter. The smaller tumor which measured 0.5 cm was attached to the right vocal cord by a short, thin pedicle. Both were round, grayish-rose in color, and smooth. On inspiration they were drawn downward toward the glottis and rose to the level of the vocal cords on expiration. The mobility of the larynx was normal, and there were no other laryngological abnormalities.

Both tumors were removed and proved to be granulomas. The larger one lacked protective epithelium. The granulation tissue was undifferentiated and fibrotic. The smaller tumor was covered with pavement cell protective epithelium. It was ulcerated and contained a central fissure and a nodule of granulated tissue.

Recovery was complete, and the patient's voice became normal. The tumor was attributed to trauma caused by the intubation.

In the 25 cases of laryngeal granuloma following intubation reported up to 1951, the duration of the anesthesia varied from fifty-five minutes to five hours. The hoarseness began as early as ten days or as late as seven months, but usually one or two months following the operation. In a few cases there was complete aphonia and dyspnea if the granuloma was large. In about fifty per cent the lesion was bilateral. In nine cases the granuloma recurred following extirpation.

Munyo considers the principal etiologic factor to be traumatic pressure exerted by the tube upon the posterior commissure, which is especially vulnerable, since it has no muscle or fibrous tissue. The trauma results in ulceration of the superficial mucosa followed by granulations. The slowly growing tumor is sessile at first, but becomes constricted at the base forming a pedunculated mass. Constitutional factors may predispose to the tumor formation by rendering the larynx vulnerable to trauma. These include debility, avitaminosis, anemia, alcoholism, and atrophy of the mucosa in the aged. The most characteristic symptom is hoarseness.

It is proposed that the Magill tube with its single curve, which does not conform to the lumen of the passage, be replaced by one with a double curve, or that smaller tubes be employed and that the duration of the anesthesia be curtailed.

HIGBEE.

Congenital Laryngeal Membrane.

Ruis, M.: Ann. Oto-rino-laryng. 23:18, 1953.

A sister and a brother six and four years respectively, both presented a history of symptoms of suffocation and cynosis at birth. They had not cried normally. When examined, they had hoarse voices and a tendency to suffocate when they cried or exercised. There was also persistent cough. The girl was a Mongolian type.

In both cases, laryngoscopic examination under general anesthesia revealed a congenital laryngeal membrane in the anterior half of the glottis between the vocal cords. X-ray examination of the head revealed no structural defects; the sella turcica was normal.

There was no familial history of laryngeal disturbances. The parents were healthy and were not related. There were, however, two instances of mongolism among the mother's antecedents.

A girl seventeen years of age is also cited who had been hoarse since birth. Her mother and father were uncle and niece. The girl had malformed ears with small auricles, atresia of the passages but no actual obstruction and an abnormally small bony orifice which allowed no access to the tympanum. The hard palate was deformed and the dental arch was V-shaped. However, the nasopharynx was normal and nasal respiration was not seriously affected. A white transparent membrane was found to occupy two-thirds of the anterior space between the vocal cords. The posterior border was concave with folds which disappeared below the glottis on phonation. A similar membrane had been surgically removed about four years previously but had recurred in the same location.

Of the 133 cases of laryngeal membrane reported prior to 1942, 75.2 per cent involved the vocal cords, 7.5 per cent the region below the glottis, 1.5 per cent that above the glottis. In 3.7 per cent of the cases the posterior wall of the laryngeal cavity was affected and in 5.26 per cent there was complete atresia.

Histologic examination of the excised membrane revealed thick fibrous connective tissue, mucous glands, elastic fibers and fat. In a few instances papillomas were present. The tissue was grayish white, yellowish or pink.

The condition appears to be more common in females than in males. In many patients the dyspnea due to the obstruction is complicated by suffocation, dysphagia and raucous breathing.

Various forms of treatment have been employed. These include: incision, surgical extirpation, galvanocauterization, fissurization, tracheotomy and dilatation with a rubber tube, extirpation followed by a Thiersch graft or insertion of a silver wire (Haslinger) between the vocal cords in the anterior commissure attached to the thyroid cartilage or of a tantalum plate (McNaught), following partial removal of the thyroid cartilage. Haslinger's procedure causes less trauma but is more difficult than the other technics.

The author calls attention to the hereditary nature of the condition in his cases and to the possible etiologic importance of consanguinity of the parents.

HIGBEE.

MISCELLANEOUS

The Sympathetic Posterior Cervical Syndrome.

Gros, J. C.: Rev. Cubana Oto-rino-laringol. 2:8:189, 1953.

Little is known regarding the pathologic anatomy of non-infectious conditions of the cochleovestibular labyrinth. In 1925 Barré first described a case of recurrent headaches, mainly occipital, disturbances of equilibrium, tinnitus, pain behind the eye balls, with temporary decrease in vision, relieved by prolonged application of warm water. The symptoms suggested involvement of the sympathetic system, especially of the vertebral nerves of the cervical region. This was confirmed by the roentgenographic evidence of osteophytic lesions of the cervical spine and loss of the anterior concavity of the vertebral column.

The vasomotor regulation of the median and lower portions of the vertebral arteries is the function of the vertebral nerves, the postganglionic branches of the stellate and intermediate ganglia of the neurovegetative system situated on both sides of the point of origin of the artery. Arthropathy results in circulatory changes, usually bilateral. The anterior cervical sympathetic nerve forms an anastomosis with the vascular nerves of the upper portion of the vertebral artery. Thus the vasomotor regulation of the blood-vessels of the labyrinth corresponds to that of the cerebral vessels. Another factor may be the CO_2 tension in the blood.

Pathologic changes may occur at the level of the fifth and sixth, or more probably the first and second vertebrae, where the artery is most exposed, due to its double curvature at this point.

Etiologic factors may be cervical arthrosis, lesions of the structures surrounding the vertebral artery and its periarterial sympathetic innervation, cervical rib, injuries to the discs, cancer of the cervical lymph-nodes, foreign bodies, or lesions of the pulmonary apex.

The most frequent symptoms are headache, vertigo, auditory and visual disturbances. The headache is persistent; it may range from a sensation of emptiness or of heaviness to severe pain, usually in the occipital region, and exacerbated by movements of the head and neck. The vertigo is constant, and may consist of a sense of insecurity or instability, but more frequently it is rotatory, and is increased by flexion or extension of the head and neck.

Vestibular symptoms include a positive Romberg reaction, sometimes spontaneous nystagmus, or deviation when the index finger test

is employed. The caloric test is generally normal, but there may be exaggerated reaction to slight stimuli. Exploration of the cervical region causes pain in the cervical insertions of the sternocleidomastoid and trapezius muscles, and in the spinal apophysis of the fourth and fifth vertebrae and in the vertebral canals.

The auditory symptoms are tinnitus and earache, in some cases auditory hyperacuity, in others perception deafness, probably due to a degenerative organic lesion. In cases of Ménière's disease, infiltration of the posterior cervical sympathetic nerve, or stellectomy, may be beneficial. There is usually osteoarthritis of the fifth and sixth vertebrae.

Visual symptoms include pain behind the eye balls, a sensation of backward traction of the eyes, temporary decrease in visual acuity.

Secondary symptoms are a "pecking" or painful sensation of the face, facial vasomotor disturbances in association with the vertigo, unilateral or bilateral spasms of the facial muscles, paresthesia of the ophthalmic region, and of the pharynx, resulting in aerophagia and eventually in atrophy of the pharyngeal musoca and vocal disturbances.

Psychic manifestations may occur, in the form of extreme asthenia, fatigability, and an anxiety neurosis sometimes leading to suicidal attempts.

These varied symptoms involving several regions can be accounted for only by circulatory disturbances located in the lateral portion of the bulbo-protuberance.

Treatment is as varied as the symptoms. Traction of the neck may relieve the vestibular symptoms. Roentgenotherapy of the posterior cervical area (250 r two or three times a week) has also been employed. Exacerbation of the headache following the initial irradiations is a good prognostic sign.

Surgical treatment consists in correction of the vertebral discs, resection of cervical rib, or freeing of the vertebral artery if it is compressed by fibers of the anterior scalenus muscle. Blocking of the stellate ganglion with novocain may cause a temporary Claude-Bernard-Horner syndrome, indicating that neurotomy of the vertebral nerve (Leriche) may prove successful, or that stellectomy is indicated, as is the case in Ménière's disease.

HIGBEE.

Cortisone and Acth In Otorhinolaryngology.

Garcia De Dios, E. P.: Acta Oto-Rino-Laringol., Ibero-Amer. 4(No. 3):180, 1953.

Cortisone and ACTH have no specific effect upon microorganisms or toxins. Their function is to modify the response of the organs and tissues to microbial or toxic agents and to inhibit allergic or inflammatory reactions. They are contraindicated in virulent infectious diseases. Their effect in reducing fever, local inflammation and pain may even mask and aggravate a latent disease. Due to their toxicity in some cases, the hormones must be used with great caution, especially if high dosages are employed. They are most effective in acute conditions of short duration and with a marked organic reaction. In allergic nasal conditions resulting in catarrh, fever and vasomotor rhinitis, the beneficial symptomatic effect is rapid and the sensitivity to allergenic agents in the air or in foods is reduced. Nasal polyps decrease in size or disappear but tend to recur. An average dose of 100 mg per day of ACTH results in relief of the respiratory obstruction. However, a second course of treatment is frequently less effective. The best results are obtained if the hormones are used as adjuvants to medical, surgical or specific anti-allergic treatment.

The hormones increase the local defense against some but not all disease agents. In a case of Streptococcus hemolyticus infection of the throat, mitral systolic murmur, lobar pneumonia, pleural effusion, anemia, marked neutrophilic leucocytosis and generalized toxic symptoms, cortisone resulted in rapid relief of symptoms. However, it is not uniformly successful in combatting tonsillitis, exudative streptococcic pharyngitis and the resultant acute rheumatic fever. In a case of agranulocytosis following sulfadiazine, sulfamezathine and sulfamerazine, the administration of 500 mg of ACTH in the course of seven days increased the number of leucocytes from 450 to 9,500 and saved the life of the patient. In another case ACTH relieved agranulocytosis after penicillin, blood transfusions, vitamin C and B complex, iron sulfate, folic acid and streptomycin had proved ineffectual.

Reports differ as to the success of the hormones in tuberculosis of the larynx. ACTH relieved the active symptoms but they recurred on cessation of treatment.

In disturbances of the ear, the hormones have been used successfully following fenestration. Due to their inhibition of osteogenesis and granulation tissue, they aid in maintaining the permeability of the

opening made in the semicircular canal. Good results have also been reported in idiopathic granuloma of the midline tissues of the nose, pharynx and larynx, which is usually fatal. In one case an initial dosage of 300 mg of cortisone, followed by 100 mg every 24 hours in divided doses for a period of 6 weeks, resulted in rapid regression of symptoms.

The consensus of opinion is that these hormones have little value in otorhinolaryngologic conditions, excepting those on an allergic basis.

The author warns against indiscriminate and empirical use of these agents due to the danger of toxic sequelae. They should be employed only as emergency measures when other medication has failed or in conjunction with specific treatment and only in conditions in which their efficacy has been established, such as agranulocytosis and idiopathic granuloma.

HIGBEE.

J.-M. LeMEE

1880-1954

Doctor Jacques LeMée, Chief of the Otolaryngological Service of the Hôpital des Enfants Malades, Paris, died there on the twenty-sixth of March.

Doctor LeMee was well known to many American otolaryngologists having visited this country on several occasions, and to many American patients through his connection with the American Hospital at Neuilly.

He was at one time President of the Société de Laryngologie des Hôpitaux de Paris and will be remembered as one of the foremost interpreters of American otolaryngological methods to the French.

Books Received

Fundamentals of Otolaryngology (Second Edition).

By Lawrence R. Boies (and eight associates). 8 vo., cloth, xx+487 pages, 197 illustrations. W. B. Saunders Co., Philadelphia, 1954.

This new second edition of Boies' popular text, following only four years after the first, is in all respects a most commendable work. It reflects the high teaching standards of its authors in many ways. The fact that they are writing for the undergraduate student does not tempt them to slight the subject matter in any degree; on the contrary there is a satisfying completeness about everything they present. As it should be, in the case of a text for a beginner, divergent views on debatable subjects are presented dispassionately, but the student always receives the benefit of the authors' own conclusions with the reasons therefor. As before, the typography and the illustrations are superb.

The Dynamics of Virus and Rickettsial Infections (International Symposium).

Edited by Frank W. Hartman, M.D., Frank L. Horsfall, Jr., M.D., and John G. Kidd, M.D. xii+461 pp., Octavo, cloth, illustrated. The Blakiston Company, Inc., New York, 1954. (Price $7.50)

The collected proceedings of a symposium on the subject sponsored by the Henry Ford Hospital in October 1953. It contains 33 papers, with discussions, collected into five groups: the Mechanisms of Virus and Rickettsial Infections; Ecology and Pathogenesis; Mechanisms of Immunity; Laboratory Diagnosis; and Approaches to Prophylaxis and Therapy. Heavy reading, for the otolaryngologist, but rewarding.

Physiological Acoustics.

By Ernest Glen Wever, Princeton University and Merle Lawrence, University of Michigan. Royal 8 vo, cloth, illustrated, xii+454 pp. Princeton University Press, Princeton, N. J., 1954. (Price $10.00)

This work deals with the ear as an acoustical instrument from beginning to end. Including as it does the anatomy and the mechanics of the middle and inner ear there is much that is familiar to the otologist, to whom it will be useful chiefly as a reference book, for it contains also much critical material in the field of perception, distortion and auditory theory. An admirable text for the audiologist.

Auditory Disorders In Children—A Manual for Differential Diagnosis.

By Helmer R. Myklebust, Professor of Audiology, School of Speech Professor of Otolaryngology, School of Medicine and Director, Children's Hearing and Aphasia Clinic Northwestern University. xiii+367 pp. Crown 8 vo., cloth, numerous tables. Grune and Stratton, Inc., New York. (Price $6.00)

A very complete treatment of the subject under fourteen chapter headings. The sections devoted to examination, diagnosis and classification are especially useful.

1954 Medical Progress—A Review of Medical Advances During 1953.

By Morris Fishbein, M.D. 8 vo., cloth, x+345 pp. The Blakiston Company, Inc., New York.

A collection of twenty short chapters by 28 authors dealing with recent progress in the several divisions and sub-divisions of medicine.

Intended as a reference book, the work has to our mind a fundamental shortcoming: references in the bibliography, which is copious, are given *without their titles or even their authors,* confronting the student with the dreary task of rummaging through the text for everything he wants, which even then gives him no hint whether a particular article is a fine fat dissertation on his subject or merely contains a passing reference to it.

Die Mund- und Rachenkrankheiten (Klinik und Therapie) Ein Leitfaden fur Arzte und Studierende. (Diseases of the Mouth and Pharynx, a guide for physicians and students.)

By Prof. C. R. Griebel. 8 vo., cloth, 140 pages, 42 illustrations, some in color. George Thieme, Stuttgart. (Price $6.90)

Die Objektive Stereoskopie an Roentgenbildern, Eine Diagnostiche Methode. (Objective Roentgenological Stereoscopy, a Diagnostic Method.)

By Prof. A. Hasselwander, Arlaching-Chiemsee. 8 vo. cloth, 187 pages, 125 illustrations. George Thieme, Stuttgart. (Price $6.40)

La Voix.

Collected papers of an International Course on Phonology and Phoniatry, held in Paris in March, 1953. Large 8 vo., pp. 434, figs. 300, Librairie Malone, Paris. (Price 5,000 Frs.)

These papers constitute a volume of contemporary European thought on a little explored subject. Twenty-six contributors; French, with a few exceptions. Handsomely printed (In French).

Notices

SIXTH INTERNATIONAL CONGRESS OF OTOLARYNGOLOGY

May 5-10, 1957 are the dates finally selected for the Sixth International Congress of Otolaryngology. The sessions will be held in Washington, D. C. with headquarters at the Statler Hotel. Plans for the scientific programs and for the accomodation and entertainment of the visiting members will be announced.

Paul H. Holinger, M.D.
Secretary General
700 N. Michigan Ave.
Chicago 11, Illinois

Arthur W. Proetz, M.D.
President

AMERICAN OTOLOGICAL SOCIETY

At the annual meeting of the American Otological Society, Inc., the following officers were elected:

President: D. E. Staunton Wishart, M.D., 170 St. George Street, Toronto 5, Canada.

Vice President: William J. McNally, M.D., 1509 Sherbrooke St. West, Montreal 25, Canada.

Secretary-Treasurer: John R. Lindsay, M.D., 950 East 59th Street, Chicago 37, Ill.

Editor-Librarian: Henry L. Williams, M.D., Mayo Clinic, Rochester, Minn.

The next annual meeting of the American Otological Society, Inc., will be held at the Hollywood Beach Hotel, Hollywood, Florida, March 17-18, 1955.

The Award of Merit, consisting of a Silver Medal, a scroll and an honorarium of one thousand dollars was given to Stacy R. Guild, Ph.D., of Baltimore, Maryland, in recognition of his many contributions in the field of research in otology during the past years.

AMERICAN LARYNGOLOGICAL ASSOCIATION

At the 75th Annual Meeting of the American Laryngological Association held at Boston, Mass., on May 27 and 28, 1954, the following officers were elected:

President: Henry B. Orton, Newark, N. J.

First Vice-President: James H. Maxwell, Ann Arbor, Mich.

Second Vice-President: Clyde A. Heatley, Rochester, N. Y.

Secretary: Henry P. Schenck, Philadelphia, Pa.

Treasurer: Fred W. Dixon, Cleveland, Ohio.

Librarian, Historian and Editor: Bernard J. McMahon, St. Louis, Mo.

Dr. Louis H. Clerf of Philadelphia was presented with the deRoaldes gold medal.

Dr. Henry B. Orton of Newark, N. J., was presented with the Newcomb Award.

The next Annual Meeting of the American Laryngological Association will be held at the Hollywood Beach Hotel, Hollywood, Florida, on March 13 and 14, 1955.

AMERICAN BOARD OF OTOLARYNGOLOGY

The American Board of Otolaryngology will conduct the following examinations:

September 13-17, 1954, in New York City, at the Waldorf Astoria Hotel.

March 6-10, 1955, in Richmond, Virginia, at the Hotel Marshall.

AMERICAN LARYNGOLOGICAL ASSOCIATION

CASSELBERRY PRIZE

A sufficient sum having accrued from the Casselberry Fund for encouraging advancement in the art and science of Laryngology and Rhinology, this sum is now available, in part or as a whole, for a prize award. Theses must be in the hands of the Secretary, Dr. Harry P. Schenck, 326 South 19th Street, Philadelphia, Pa., before March 1, 1955.

Copies of the Transactions of the American Laryngological Association are available for general distribution at $8.00 a copy. Please send request with check to:

Dr. Bernard J. McMahon,
Editor Transactions
8230 Forsyth Blvd.
Clayton 24, Mo.

ACADEMY HOME STUDY COURSE

The Home Study Courses in the basic sciences related to ophthalmology and otolaryngology, offered as a part of the education program of the American Academy of Ophthalmology and Otolaryngology, will begin on September 1 and continue for a period of ten months. Registrations must be completed before August 15. Detailed information and application forms may be secured from Dr. William L. Benedict, the executive secretary-treasurer of the Academy, 100 First Avenue Building, Rochester, Minnesota.

UNIVERSITY OF PENNSYLVANIA

Announcement is made of the personal fundamental course in Bronchology, Esophagology, Gastroscopy and Laryngeal Surgery at the Graduate School of Medicine, University of Pennsylvania. The course begins September eighth and continues through September nineteenth.

Courses are scheduled usually in January, June and September avoiding conflict with the meeting dates of the National Medical Societies.

Application may be made to Dr. Aims C. McGuinness, Dean, or to Dr. Gabriel Tucker, Chairman of the Department of Bronchology, Esophagology, and Laryngeal Surgery.

TULANE UNIVERSITY OF LOUISIANA SCHOOL OF MEDICINE

The three year residency in otolaryngology offered at Charity Hospital of Louisiana at New Orleans on the Tulane University of Louisiana School of Medicine service is designed to qualify the holder for the examinations of the American Board of Otolaryngology and the practice of all phases of otolaryngology and endoscopy.

Candidates must be graduates of a class A medical school and must have completed a minimum of one year of general internship. An additional year of residency in internal medicine or general surgery is desirable but not essential.

All work is under the direct supervision of members of the Tulane Department of Otolaryngology, who are also members of the Charity Hospital Otolaryngological Staff; they are available at all times for instruction and guidance. Basic sciences are offered throughout each year of the residency during the academic year. The resident also participates in the program of the Speech and Hearing Center at the Tulane University School of Medicine.

The hospital year extends from July 1 of one year to June 30 of the following year.

Applications should be addressed to the Chairman of the Department of Otolaryngology, Tulane University of Louisiana School of Medicine, 1430 Tulane Ave., New Orleans 12, Louisiana.

UNIVERSITY OF ILLINOIS

The Department of Otolaryngology, University of Illinois College of Medicine, announces its basic science course in otolaryngology offered by its affiliated hospitals. This combined postgraduate course and residency will begin its 1954-55 session on July 1, 1954. Other openings occur throughout the year. Residencies are available at either the Research and Educational Hospital or the Illinois Eye and Ear Infirmary, or a continuation of the training program may be arranged for the Veterans Administration Hospital at Hines.

A stipend is offered on the following basis:

First year residency	$1320	annually
Second year residency	1620	annually
Third year residency	1920	annually

Application forms are available on request to the Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12.

COLBY COLLEGE COURSE IN AUDIOLOGY

For the second consecutive year Colby College in Waterville, Maine will present August 8-14 its course "Audiology for Industry."

This course is designed to enable industrial physicians and plant engineers to determine noise levels which might result in acoustic trauma and to set up programs to protect the ears of workers in heavy industry.

The faculty will consist of leading authorities in this field.

Registrants will live on the college's new Mayflower Hill campus. The tuition fee of $200 includes board and room. Applications should be made to Ralph S. Williams, Director, Adult Education, Colby College, Waterville, Maine.

FOURTEENTH JAPAN MEDICAL CONGRESS

The Fourteenth Japan Medical Congress will be held in Kyoto, April 1-5, 1955. Particulars may be had of the Secretary General, Mitsuharu Goto, University Hospital Kyoto University, Kyoto, Japan.

PORTUGESE OTORHINOLARYNGOLOGICAL SOCIETY

On March 20 the Sociedade Portuguesa de Otorrinolaringologia e de Bronco-esofogologia was founded, and held its first meeting in Lisbon under the presidency of Dr. Alberto Luís de Mendonça. The Secretary is Dr. António da Costa Quinta, Avenida de Liberdade 65, 1° Lisbon.

DINNER OF MILITARY OTOLARYNGOLOGISTS AND OPHTHALMOLOGISTS

The Society of Military Otolaryngologists and the Society of Military Ophthalmologists will hold a joint dinner meeting at the time of the XVII International Congress of Ophthalmology and the annual meeting of the American Academy of Ophthalmology and Otolaryngology in New York City in September.

Cocktails and dinner will be served at 6 p.m. on Tuesday, September 21, 1954, in the South and Center Lounges, Shelton Hotel, Lexington Avenue and 49th Street, New York City (across the street from the Waldorf-Astoria).

All members, otolaryngologists and ophthalmologists on active duty with the Armed Forces, are invited to attend. Application should be made to Colonel J. H. King, Jr., Secretary-Treasurer, Society of Military Ophthalmologists, Eye Clinic, Walter Reed Army Hospital, Washington 12, D. C.

PAN-AMERICAN SURGICAL ASSOCIATION

Doctors are cordially invited to attend the Sixth Congress of the Pan-Pacific Surgical Association to be held in Honolulu, October 7-8, 1954.

For further information, please write to F. J. Pinkerton, M.D., Director General, Pan-Pacific Surgical Association, Suite 7, Young Building, Honolulu, Hawaii.

IV INTERNATIONAL CONGRESS

There are a few copies of the Proceedings of the 4th International Congress of Otolaryngology still available for purchase.

The publication contains all of the numerous papers, and is well produced. Copies may be had, at Five Guineas, from

The Secretary
British Medical Journal
B. M. A. House
Tavistock Square
London, W. C. 1.

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The management of the ANNALS desires to buy, at $1.50 each, copies of the following numbers which are out of print:

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OF THE

NATIONAL OTOLARYNGOLOGICAL SOCIETIES

American Academy of Ophthalmology and Otolaryngology

President: Dr. Derrick Vail, 700 N. Michigan Blvd., Chicago 11, Ill.
Executive Secretary: Dr. William L. Benedict, Mayo Clinic, Rochester, Minn.

American Board of Otolaryngology

President: Dr. Frederick T. Hill, Professional Bldg., Waterville, Maine.
Secretary: Dr. Dean M. Lierle, University Hospital, Iowa City, Iowa.

American Broncho-Esophagological Association

President: Dr. Edwin N. Broyles, 1100 N. Charles Street, Baltimore, Md.
Secretary: Dr. F. Johnson Putney, 255 S. 17th St., Philadelphia 3, Pa.
Meeting: Statler Hotel, Boston, May 25th and 26th, 1954.

American Laryngological Association

President: Dr. Gordon F. Harkness, 2410 River Drive, Davenport, Iowa.
Secretary: Dr. Harry P. Schenck, 326 South 19th St., Philadelphia, Pa.
Meeting: Boston, Mass., May 28 and 29, 1954.

American Laryngological, Rhinological and Otological Society, Inc.

President: Dr. Francis LeJeune, Prytania and Olive Sts., New Orleans, La.
Secretary: Dr. C. Stewart Nash, 708 Medical Arts Bldg., Rochester, N. Y.
Meeting: Boston, Mass., May 25-27, 1954.

American Medical Association, Section on Laryngology, Otology and Rhinology

Chairman: Sam H. Sanders, M.D., Memphis, Tenn.
Secretary: Hugh A. Kuhn, M.D., Hammond, Ind.
Meeting: San Francisco, June 21-25, 1954.

American Otological Society

President: Dr. Frederick T. Hill, Professional Bldg., Waterville, Maine.
Secretary-Treasurer: Dr. John R. Lindsay, 950 East 59th St., Chicago 37, Ill.
Meeting: Boston, Mass., May 23 and 24, 1954.